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INTUBATION STUDIES OF THE HUMAN SMALL INTESTINE

V. THE MOTOR EFFECTS OF SINGLE CLINICAL DOSES OF MORPHINE SULPHATE IN NORMAL SUBJECTS*

By W. OSLER ABBOTT, M.D., *and* EUGENE P. PENDERGRASS, M.D.
PHILADELPHIA, PENNSYLVANIA

INTRODUCTION

THE use of opium to control diarrhea is probably as old as cholera in China, yet we still know little of how the constipating action is produced. In all hollow viscera the normal movement of contents depends on reciprocal contraction and relaxation, a dominance of either phase impeding progress. Expressing these contrasting possibilities are the two current theories regarding the mode of action of morphine upon the essential unit of the digestive tract, the small intestine. Magnus,[3] Schwenter,[11] Schapiro,[10] Mahlo,[4] and Pancoast and Hopkins,[8] writing in the first quarter of this century, from roentgenologic evidence concluded that in man and animals either no small intestinal effect occurs or one characterized by relaxation and inactivity.† More recently Plant and Miller,[9] Gruber and Robinson[2] and Orr and Carlson[7] stated, on the basis of intraintestinal balloon experiments on unanesthetized Thiry-Vella loop dogs, that the characteristic effect is contraction resulting in increased tonus and activity, two of the group claiming that in man essentially the same result occurs. Thus two divergent views have been arrived at by the use of two unrelated methods of study: one by roentgenological investigation in man and animal; the other by the balloon technique in the surgically disarranged intestine of dogs, and occasionally through fistulae in diseased human subjects. The obviously desirable procedure of applying both methods simultaneously to normal men has only recently been made possible by the introduction of a technique for human small intestinal intubation by Miller and Abbott.[5,6] To aid in clarifying the clinical indications for this drug, we have attempted such a procedure, limiting ourselves to doses and methods of administration in actual daily use. Our results show that both of the seemingly opposed views on the behavior of the small intestine in response to this drug are in part correct.

METHOD

(*a*) *Subjects.* The subjects for these experiments were in the main ambulatory ward patients having mild complaints not grossly affecting the digestive tract. A few

† The early literature on the gastrointestinal effects of morphine has been so thoroughly reviewed by Plant and Miller, Gruber et al and by Orr and Carlson that further repetition seems unnecessary.

* From the Gastrointestinal Section of the Medical Clinic and the Department of Radiology of the Hospital, University of Pennsylvania. Read at the Thirty-sixth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 24–27, 1935.

observations were made upon hired normal subjects in the course of a series of intubations for other purposes. A total of 34 experiments was performed upon 31 individuals, 2 only receiving the drug upon more than one occasion. Due precautions were taken to prevent the subject from identifying the drug injected.

(*b*) *Technique.* Group 1: Intraintestinal Balloon Studies.‡ Four experiments were carried out with twin balloons of thin rubber

FIG. 1. The normal appearance of intubated small intestine. The motility and the mucosal pattern are normal in spite of the presence of a tube, as judged by a control study of the same individual. H. Z.: A healthy white male, aged thirty-one, took the tube fasting at 8:30 A.M. and a large opaque meal at 1:00 P.M. After two hours and fifty minutes this roentgenogram was taken.

which were placed in any desired region of the bowel as described by Miller and Abbott.[5,6] Each balloon, connected by a separate lumen of the tube to a spirometer type volume recorder, could be expanded to a maximum of 50 c.c. by a 12 to 15 cm. water column inserted in the otherwise air-filled system, while to collapse the balloon a force sufficient to sustain a 22 to 25 cm. water column was required. Thus in the empty intestine, this apparatus records both volume and pressure changes within these limits. In the full intestine, however, a column of incompressible content will transmit pressure so that the contraction of one loop may distend another. Should a balloon lie in the second loop, the force which tends to expand the gut will tend to empty the balloon. A lengthening of the muscle may then be accompanied by a rise rather than a fall in the tracing. In this situation the balloon measures pressure and the roentgenoscope measures volume.

In either event contractions could be recorded and a distinction between those of the peristaltic and of the segmental types could be drawn as in records from Thiry-Vella loops. Roentgenoscopic observations, however, showed that waves apparently "peristaltic" did not always move contents and that waves of a "segmental" type might be appearing coincidentally with active motility. Moreover, our studies of segmental waves under divers conditions indicate that the rate varies inversely with the amplitude of the waves and that the amplitude is dependent on the intraintestinal pressure. When that equals 15–20 cm. of water the amplitude is usually maximum, decreasing progressively with any divergence from that level. For this reason we have used the term peristalsis and segmentation when it seemed appropriate, but in general have described contraction under one heading.

Group 2: Combined Balloon and Roentgenologic Studies. Twenty-six experiments were performed upon 22 subjects. In these the same technique of intubation as discussed in Group 1 was used, but in addition the subject was kept upon a roentgenoscopic table throughout the entire period of the experiment and sufficient barium sulphate given at appropriate times to allow a roentgenological study of intestinal activity (Fig. 1). When a barium meal was given and the region of the intestine under

‡ For much of the apparatus used in these studies we are indebted to the Department of Pharmacology of this University.

investigation appeared full, the balloon record was interpreted in terms of pressure only; if, however, that region of the gut had emptied itself or if but a few cubic centimeters of dry barium sulphate powder had been given the record was interpreted in terms of both pressure and volume, the gut being considered empty.

Group 3: Roentgenologic Studies after a Barium Meal. Four patients were studied, each receiving two complete roentgen examinations of the stomach and small intestine, both by roentgenoscopy and by roentgenograms. On one occasion this was done with the subject in the normal fasting state, and at another time after a subcutaneous injection of morphine sulphate. The observations were continued for three hours, 15 roentgenograms being made in this period. Every precaution was taken to see that for each case the control and the experimental procedures should be identical.

(*c*) *Drug.* The preparation of morphine sulphate used was that of Sharp and Dohme Company put up in standard packages of 1/6 and 1/4 grain tablets for hypodermic use. The doses ranged from 1/6 to 1/2 grain.

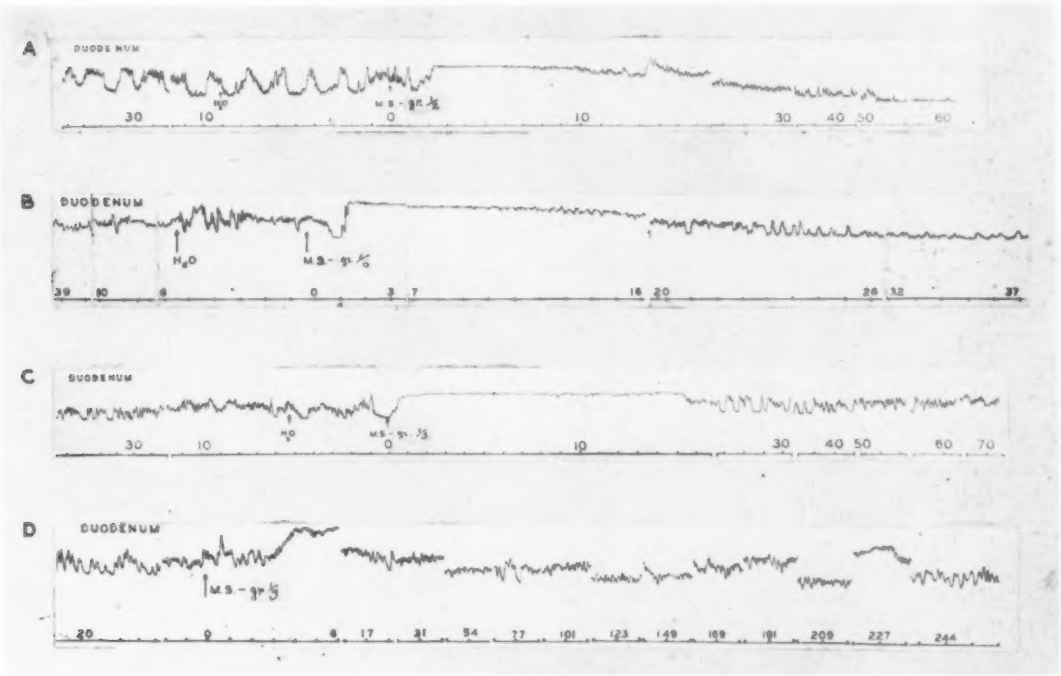

Fig. 2. *Balloon tracings from the duodenum.* Using an air conduction system under 12 to 22 cm. of water pressure and spirometer type recording instruments, the effects of control injections of water and of morphine doses ranging from $\frac{1}{4}$ to $\frac{1}{2}$ grain were studied. The time in minutes is indicated by the figures along the base line. *A.* A white male, D.P., aged forty-four, having Buerger's disease with an ulcer of the foot but no digestive symptoms, was given a barium meal fifty minutes before the drug. This had completely left the stomach and duodenum forty minutes after the injection. *B.* A white male, M.T., aged forty-five, having benign hypertension and slight constipation, was studied in the fasting state. *C.* A white woman, M. McC., aged forty, having a small uterine fibroma but no digestive symptoms, was given a large barium meal forty minutes before the drug and her stomach had not completely emptied at the conclusion of the experiment. *D.* A healthy black boy, J.R., aged twenty-three, was studied in the fasting state.

RESULTS

General Considerations. The 34 experiments performed, since they were designed to bring out different aspects of morphine

action at different points throughout the small intestine, varied widely in detail one from another. The results are therefore presented as a sequence of events, exceptions to the usual response being pointed out as they occurred. The differences in effect between small (1/6 grain) and large (1/3 grain) doses were solely a matter of degree, so that no subdivision on the score of dosage will be made.

times even of 40 cm. of water. This reaction was indicated on the moving drum by an abrupt change in the tracing from the control pattern to a flat topped plateau rising sharply but terminating gradually (Figs. 2 and 3).

Roentgenoscopy indicated a normally active duodenum which, upon the injection of the drug, rapidly emptied itself of contained barium and subsequently trans-

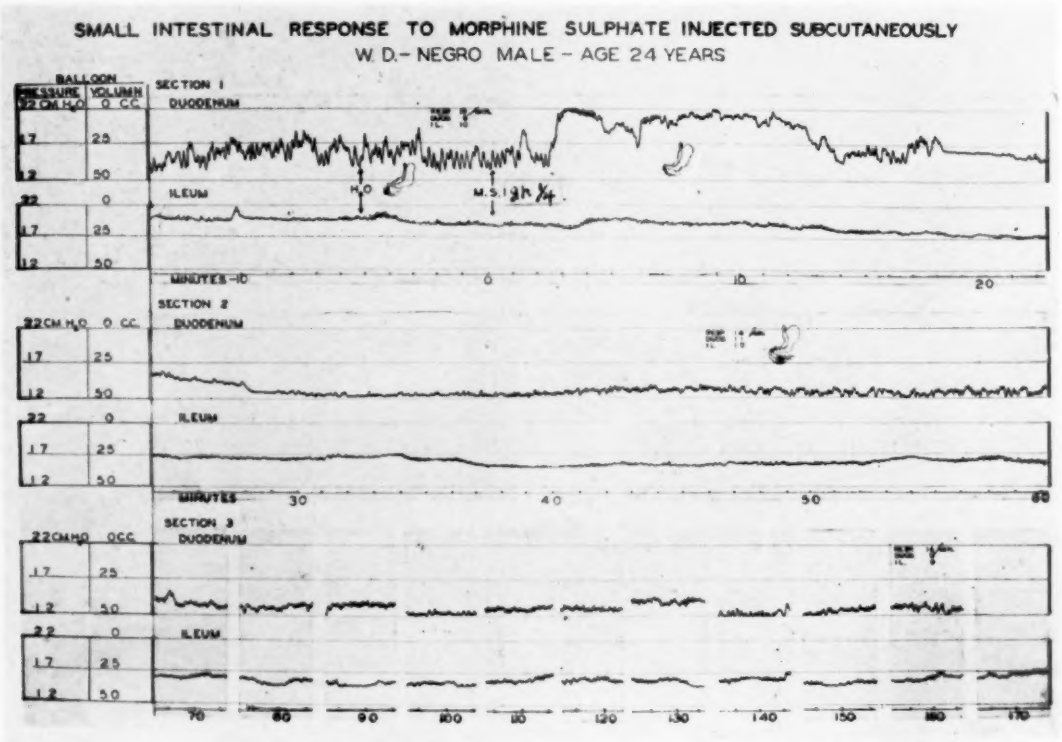

FIG. 3. *Simultaneous balloon tracings from the duodenum and ileum.* These records made with duplicate apparatus record the effects of a control injection of water followed by an injection of ¼ grain of the drug upon the intestine of a healthy subject. The tracings are calibrated for balloon pressure and volume. About 8 c.c. of dry barium sulphate powder was given, enabling one to sketch the breadth of the duodenum, which was very narrow when the tracing level was high and greatly widened when the subsequent fall in level occurred. The time in minutes is indicated along the base line.

Duodenum. (a) Tonus: Within two minutes of the injection of morphine an abrupt tonic contraction took place in the duodenum distal to the cap, practically obliterating the lumen for approximately twenty minutes. No other organ of the body has in our experience shown so prompt a response to this drug. The force of the contraction was usually sufficient to empty a balloon against a pressure of 25 and at

mitted far less of it than during the control period (Fig. 4). When dry powdered barium was given instead of the liquid meal, sufficient adhered to the villi to enable one to see the duodenum as a narrow line even with the lumen obliterated. This tonic contraction, while it began at the second part, spread distally in most cases, and to some extent proximally though never in our experience involving the cap.

The dilatation which followed the initial contraction may be described as the second phase of the upper intestinal response, and is of far more practical importance, since it was often present even up to three hours after the injection. In tracings taken from fasting subjects the level of the line dropped, indicating an increase in intestinal diameter at this time (Fig. 2, *A*, *B* and *D*, and Fig. 3); in those from cases having had a barium meal, however, the record showed that no fall in intraintestinal pressure need occur with this lengthening of the muscle fibers (Fig. 2, *C*). In either case roentgenoscopy indicated a marked widening of the viscus (Figs. 3, 5 and 6). From the proximal duodenum this relaxation spread distally until much of the jejunum was involved (Figs. 6 and 7).

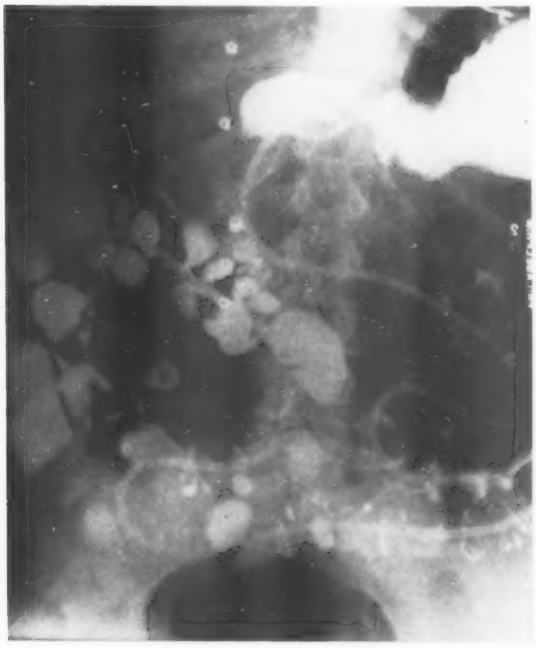

FIG. 4. *Early roentgenographic changes in the duodenum and ileum.* The appearance one hour and forty-five minutes after the first barium meal and twenty minutes after the second meal, which was accompanied by the injection of 1/6 grain of the drug. The opaque material is seen filling the stomach and duodenal cap but stopping abruptly at the descending portion of the duodenum. In the ileum the irregular dilatations giving the haustration-like appearance are especially clear. C.C.: A white woman, aged forty-eight having neurasthenia without digestive disturbances, was given the tube at 8:30 A.M. while fasting.

FIG. 5. *Later roentgenographic changes in the duodenum and ileum.* The appearance two hours and fifteen minutes after one barium meal and half an hour after a second which was accompanied by the injection of 1/3 grain of the drug. The stomach is active, the duodenal cap dilated, and the duodenum probably just beginning to dilate as the jejunum is still empty. The ileum shows the intermittent areas of dilatation. A.H.: A white male, aged twenty-six, having chronic rheumatoid arthritis but no digestive symptoms, took the tube at 8:30 A.M. while fasting.

(b) Contractions: During the control period the contractions of the duodenum were more active and more complex than those of the ileum (Figs. 2, 3 and 8). The duodenal balloons ordinarily recorded two types of wave, one a slow deep undulation of the tonus level recurring at approximately two minute intervals, the other a smaller, more rhythmical contraction superimposed upon the larger and averaging about six per minute (Fig. 2, *A*). The amplitude of the smaller waves generally rose with the larger and fell with them. It is waves of the larger type that have frequently been referred to as peristalsis, while the smaller are generally termed segmentation, though these

terms were originally applied to contractions recorded by totally dissimilar methods. This clearcut distinction in the character of the waves was by no means always apparent, however. With the injection of morphine a momentary change might occur as frequently happened after a control injection of water, but with the rise in tonus all waves were practically obliterated, This was apparently due to

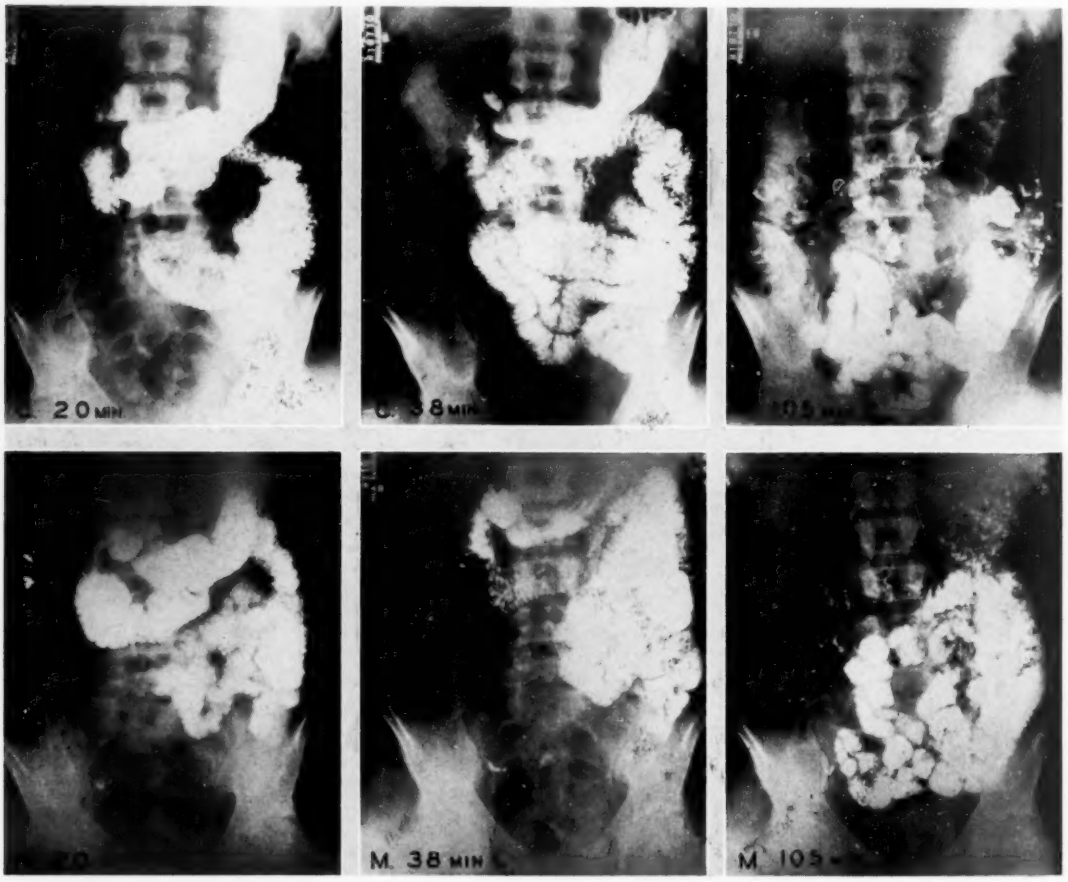

FIG. 6. *Motility changes in the small intestine.* A comparison of the progress of a barium-in-water meal throughout the small intestine under control conditions (Series C) and after $\frac{1}{4}$ grain of morphine (Series M) in W.M., a healthy white male, aged forty. *C*—20-minute film: Normal motility is present throughout the stomach, duodenum and upper jejunum. Peristalsis is active and orderly. The mucosal pattern is typical for the respective regions. *M*—20-minute film: The stomach shows active peristalsis and is propelling its contents freely as far as the distal end of the dilated duodenal cap. Here the initial tonic contraction which occurs first and continues longest at this point is beginning to relax. Beyond this region dilatation is already marked. The mucosal pattern is obscured here by the increasing depth of barium but is still discernible in the jejunum. *C*—38-minute film: Gastric peristalsis and motility are normal. The stomach is half empty. The small intestinal column has advanced through the vertical jejunal coils in the left upper quadrant well down into the horizontal coils of the mid-abdomen. *M*—38-minute film: An acceleration of gastroduodenal motility is marked, the duodenal cap remaining dilated. The stomach has almost completely emptied presumably due to lessened peripheral resistance as the jejunum is dilating and retaining the gastric content it receives rather than passing it on. Practically no barium has advanced beyond the vertical left upper quadrant coils, nor is jejunal activity apparent, though a change in the mucosal pattern is discernible. *C*—105-minute film: The opaque column has advanced normally to the lower ileum. *M*—105-minute film: Some of the barium has now advanced into the ileum, which presents the usual appearance of localized areas of dilatation, but much of the opaque meal is still present in the high jejunal coils of the left upper quadrant.

"diastole" being prevented. If, however, the pressure in the balloon was raised, small rhythmic waves appeared, having a low amplitude and a rate of about eleven per minute, or roughly double the rate of the rhythmic waves of the control period. This condition lasted throughout the period of high tonus, but as the recording lever began to fall the amplitude of the contractions rapidly increased, chiefly through a gain in the degree of relaxation. As the tonus fell below the control level, however, the "systolic" phase of the waves diminished and throughout the protracted period of low tonus the waves were, as a rule, below the amplitude of the control period. It was noteworthy also that after morphine the records rarely showed an appearance suggesting peristalsis, in spite of the fact that barium might be seen moving past the balloon (Figs. 2 and 3).

Roentgenoscopically the appearance of barium in the duodenum was unaltered by the presence of a tube (Fig. 1). Following the injection with the changes already described in duodenal caliber a disappearance or marked diminution in the waves was evident (Fig. 6, *M*-20 min.). At the time of falling tonus when the tracing showed large waves a coincident irregular fluctuation in intestinal diameter might be seen. Often there was little if any suggestion of propulsion, though at times barium might be moving rapidly from the stomach into the upper intestine. When the phase of relaxation was well established, however, small undulations were seen quite constantly in the duodenum.

Ileum. (a) Tonus: The ileum contrasted with the duodenum in its behavior both before and after the injection in that its tonus level was more stable. No immediate effect occurred and only slowly might a slight rise in tonus take place, reaching its height about fifteen minutes after the giving of the drug and thereafter declining to a level usually below that of the control (Fig. 8, *A*, *B* and *C*). At most this represented a displacement of but 10 to 15 c.c. from the balloon, or an increase in hydrostatic pressure of 3 to 4 cm. In several instances no such change occurred, one of these being a case in which constant suction was applied to the intestinal contents immediately above the ileal balloon through a separate lumen of the tube, so that if the rise in pressure was due to movement of intestinal contents down against the balloon this source of error might be eliminated (Fig. 8, *D*). In short, the level of the balloon tracing half an hour after the giving of morphine was sometimes at or slightly above the control level, but with the ileum empty it was almost always below it.

Fig. 7. *Jejunal dilatation.* The appearance forty-three minutes after one opaque meal, twenty minutes after a second and thirteen minutes after a 1/6 grain injection of morphine. The stomach and duodenal cap are well filled, the position of the remainder of the duodenum being indicated only by the presence of the tube, though this is not apparent in this plate due to overlying jejunum. The jejunum itself is beginning to dilate in an irregular fashion with a change in the mucosal pattern. R.C., a white boy, aged twenty, convalescent from acute nephritis and free from digestive symptoms, took the tube fasting at 8:30 A.M.

This variability of results was in keeping with the roentgenographic changes which took place in the appearance of barium

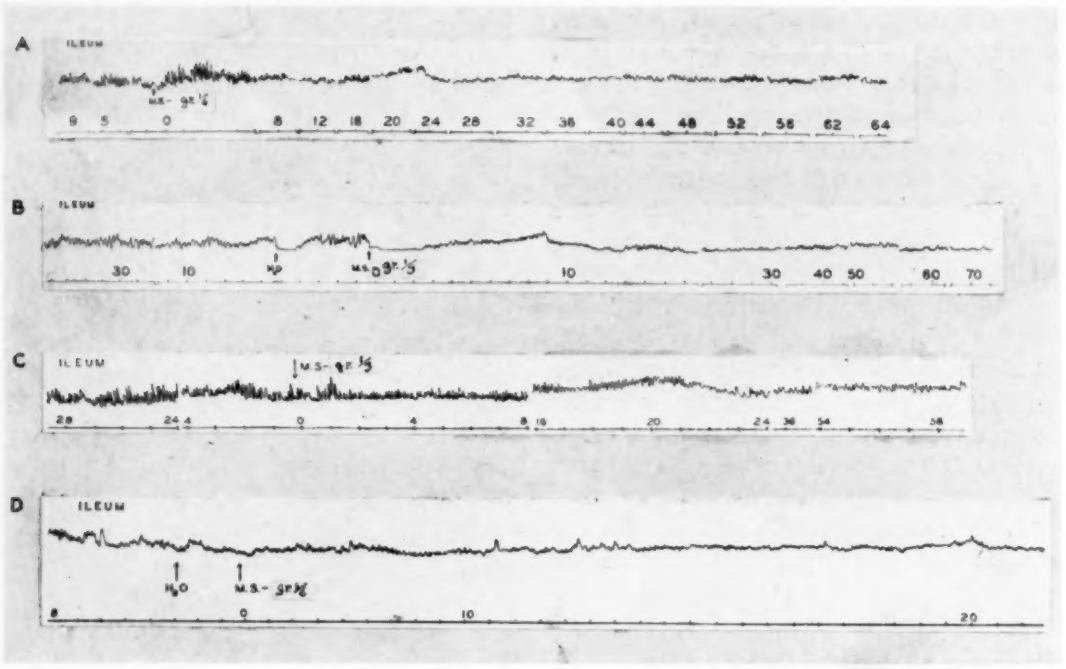

FIG. 8. *Balloon tracings from the ileum.* These records were obtained with the same technique as in Figure 2, save in Experiment *C*, in which instance a Brodie bellows was used. Doses of $\frac{1}{6}$ and $\frac{1}{3}$ grain were used. *A.* A white male, J.E., aged thirty-four, having bronchial asthma without digestive disorders, was given a large barium meal two hours before the beginning of the experiment, so that the ileum was well filled at the time the drug was given. *B.* Experiment reported in Figure 2-*C*, the tracings being taken simultaneously. *C.* A white woman, F.F., aged thirty-seven, diagnosed neurasthenia, presented slight constipation as her only digestive symptom. She received two barium meals: the first, three hours before the beginning of the experiment, had filled the ileum before the drug was given; the second was taken at the start of the examination. *D.* A white male, R.R., aged thirty, had complained of vague abdominal pain relieved by diet. Throughout the examination, which was made with the subject fasting, constant suction was applied to the intestinal lumen above the balloon to prevent the accumulation of contents. The time in minutes is indicated along the base line.

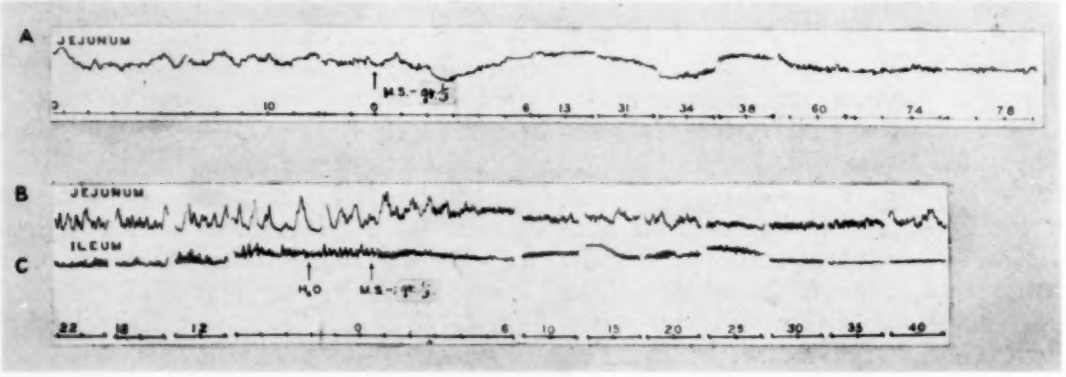

FIG. 9. *Balloon tracings from the jejunum.* The same technique was used as in Figure 2. Doses of $\frac{1}{3}$ grain of morphine were used. *A.* A white male, J.D., aged thirty-five, having Buerger's disease with ulceration of a toe; no digestive disturbances. The study was made with the patient fasting. *B.* A white woman, I.C., aged fifty, who had recovered from a mild vitamin B deficiency. The study was made with the patient fasting. *C.* The same case, a tracing from the ileum taken coincidentally. Time in minutes is indicated along the base line.

already present in the ileum at the time of the injection. The long, rather inactive coils of opaque material showed no immediate effect, but from five to fifteen minutes after the injection an agglomeration began, certain loops slowly dilating while the barium disappeared from the intervening coils. This resulted presently in an appearance simulating large opaque sausages isolated one from another. Some of these faded off indefinitely, others were abruptly terminated by a contracted area (Fig. 5). These rather stationary contractions were at times so close together as to give a haustrated appearance to the ileum, suggesting colon in outline (Fig. 4). The duration of this effect was indefinite, such an appearance at times lasting for two to three hours, the barium showing little tendency to progress in an orderly fashion yet moving frequently in a disoriented manner.

(b) Contractions: Though by roentgenoscopy of the ileum one could tell little more than that contractions were taking place, the balloon record showed a pattern quite distinct from that of the duodenum both in the control period and after the drug. Waves of the slow deep type, described from the duodenum as suggesting peristalsis, rarely occurred, nor as a rule were the smaller waves as regular in form and variable in amplitude as in the upper intestine. The waves were low, displacing but 1 to 3 c.c. of air, the rate averaging about eleven per minute. Following the injection a complete cessation of contractions, or a slight increase in their amplitude might occur, but the same was often true following a control injection of water. In general, the rate was little changed throughout the experiment but the amplitude considered over a period of an hour or two tended to decrease (Figs. 3 and 8).

Jejunum. The jejunum responded to morphine in a manner varying with the region studied. Near the ligament of Treitz a rise in tonus resembling that recorded from the duodenum occurred, but it came on more slowly and subsided sooner. From more distal segments the response more nearly resembled that of the ileum, in that little initial response was detectable but a depression of activity followed. Contractions bore much the same relation to the tonus level as elsewhere, becoming progressively less active as successive regions were studied from the duodenum to the ileum (Fig. 9).

Motility Changes in the Small Intestine as a Whole. To correlate these local responses of the different portions of the gut, the general redistribution of barium within the intestine, as recorded roentgenologically following the injection of morphine, may be described. The first effect observable was the tonic contraction of the second part of the duodenum noted above, which soon involved this whole region except for the cap. The stomach, continuing its activity, was prevented from emptying normally by high duodenal resistance. One could often see a tapering wedge of barium advancing and retreating through the pylorus and duodenal cap, only occasionally able to force a bolus throughout the remainder of the duodenum. Meanwhile the original content of the duodenum had been expelled distally toward the lower jejunum and ileum leaving a steadily increasing gap between the ends of the opaque columns (Fig. 4). This augmented the ileal content which meanwhile had assumed the "haustrated" or sausage string form described. The duodenum and upper jejunum now dilated (Fig. 6, *M*-20 min.). The stomach, working against reduced peripheral resistance, began to empty more rapidly than normal. The upper small intestine, receiving the barium into its dilated coils and failing to pass it on to the ileum, dilated (Fig. 6, *M*-38 min.) Finally we saw not only a long delay in the time required for the barium to reach the cecum, but also for the small intestine to clear itself of barium (Fig. 6, *M*-105 min.). A normal gastrointestinal roentgenographic study could not be made within twenty-four hours, and we feel that in some cases the effect of the drug is detectable for three days.

DISCUSSION

As has been stated, the previous views upon the action of morphine in man have been contradictory and both are in partial opposition to our own. The delayed emptying time and diminished motility described by the earlier writers is in agreement with our results in regard to the secondary effects. The early delay in gastric emptying they attributed to pylorospasm, presumably believing that the duodenum was empty because nothing was coming into it. Our balloon studies, however, indicate that the duodenum is empty because it is too tightly shut to receive gastric contents. The repeated passage of opaque material back and forth through the pylorus into the cap could not occur were the pylorus in spasm. It is well known that the second part of the duodenum is the most responsive portion of the digestive tract to simple irritants, and it seems likely that this effect of morphine is evidence of a similar responsiveness to parenterally administered drugs. Our observations constitute further support for the belief that the emptying of the stomach is largely controlled not by the pylorus nor the duodenal cap but by the irritability of the proximal half of the duodenum proper, a concept which would harmonize much of the conflicting evidence on the function of the pylorus.

Those who have found evidence for motor stimulation by morphine in man have presented various types of data. Probably the soundest have been the balloon studies carried on through preformed intestinal fistulae. In general, it is difficult to interpret these reports since it has not been made clear when the records represented volume changes, that is to say, were taken from a strictly empty gut, and when they represented pressure changes as would be the case when the tract contained food residue. These observations have been few in number and their duration brief with little said of the diagnosis and the time interval since the original operative procedure in most cases.

One case reported by Plant and Miller[9] showed a slow increase in ileal tonus for fourteen minutes and a fall for the next three minutes, at which time the experiment was terminated. Orr and Carlson[7] likewise studied one case of ileostomy with resultant evidence of increased activity and either a contraction of the bowel or a rise in internal pressure. How long that lasted is not stated. Dvorak et al[1] speak of "8 cases either of ileostomy or colostomy" with increased activity but no statement of the number of small intestinal fistulae in the group or the duration of the change is given. In short, the data as far as they go are not only compatible with our own but susceptible of the same interpretation.

Thin-walled hernial sacs have been observed by Plant and Miller[9] and by Orr and Carlson.[7] The former give the more detailed report, finding in each instance increased activity of the gut for some time after the injection. The appearance of "haustration" (Fig. 4 and Fig. 6, *M*-104 min.) in the ileum as we are familiar with it, plus the movement of intestinal contents as described, presumably could produce this effect, though in 3 cases of our own, huge hernias but perhaps not containing small intestine, we failed to see any change after giving the drug.

Auscultation of the abdomen has been practiced by Wilen and Dragsted,[12] by Dvorak et al[1] and by Orr and Carlson,[7] all agreeing that for a time after the injection intestinal sounds are increased in intensity. This has similarly been our experience, though we have hesitated to interpret such evidence in terms other than of activity without reference to tonus or to the progressive movement of contents.

Finally, Orr and Carlson[7] observed that ileal mucosa exposed at a fistula opening increased in activity after morphine was injected. We also have observed such an effect in one case lasting for ten minutes and then dying out, but this we believe is due to activity of the muscularis mucosae.

Such a review of the recent studies of morphine action suggests that though the interpretation is at variance with our own the evidence presented is, as far as it goes, in harmony with our findings.

SUMMARY

The first effect upon the small intestine of man of a single injection of morphine is stimulatory, producing a rise of tonus greatest in the most reactive region of the gut, the duodenum, and slight or absent in the ileum. During this period the height of contractions is diminished in proportion to the degree to which increased tonus prevents "diastole" with the usual increase in rate proportional to the reduction in amplitude. Twenty minutes later a depressant action sets in and may last for hours, the tonus falling in the sense of a lengthening of the muscle fiber. This secondary effect also occurs to a far greater degree in the duodenum than in the ileum. Contractions increase in amplitude for a brief period as the falling tonus reaches the optimum level for their occurrence and subsequently diminish roughly in proportion to the degree of fall in tonus.

The general effect of these changes is first to make the gradient of tonus steeper, causing an initial rapid downward flow of duodenal and high jejunal contents toward the ileum and then to level off the gradient, leading to a marked prolongation in small intestinal emptying time. From the broad standpoint it may be construed as further evidence that small intestinal motility is primarily related to tonus differences rather than to contraction waves, since the effectiveness of the waves seems to depend primarily upon the tonus level from which they arise.

From the practical standpoint these findings are unfavorable to the use of morphine in conditions associated with intestinal distention, unless the other advantages of the drug outweigh this aspect of its action, but no final judgment should be rendered upon so splendid a drug until the effects of repeated doses have been thoroughly studied.

CONCLUSIONS

Morphine causes in man a brief stimulation followed by a prolonged depression of small intestinal muscular contraction, the intensity of the reaction decreasing progressively from duodenum to ileum, the distal coils frequently exhibiting no reaction or merely the phase of depression.*

* For discussion see page 315.

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INTUBATION STUDIES OF THE HUMAN SMALL INTESTINE

VI. THE INFLUENCE OF VARIATIONS IN THE REACTION AND THE MOTILITY OF THE STOMACH CONTENTS ON THE REACTION AND THE MOTILITY OF THE INTESTINAL CONTENTS*

By T. GRIER MILLER, M.D., *and* W. G. KARR, Ph.D.
PHILADELPHIA, PENNSYLVANIA

INCIDENT to a study of the normal human small intestine by a method of intubation,[1,2,3,4,5] we have had occasion from time to time to make observations on individuals in whom the secretory function of the stomach under standard conditions varied beyond the recognized physiological limits. In this presentation we shall refer to four experiments on three subjects who proved, after a gruel meal, to have gastric hyperacidity, and to two experiments on true achlorhydria cases; none had a demonstrable organic stomach lesion. In each instance we shall give data on the intestinal contents under fasting conditions and after an attempt to alter the reaction, and incidentally the motility, of the gastric contents.

The six experiments have been chosen from a series of about 100 similar studies made in our clinic over a two year period. All of the intubations were performed by Abbott. The technique is difficult, time-consuming and requires much patience on the part of the investigator, but it is not so disturbing to the subject as its description may suggest. It involves the introduction of a specially developed double-lumened tube[1] with a collapsible rubber balloon connected to one of the lumina at its distal extremity. The most difficult part of the procedure is the passage of the tip of the tube from the first into the second portion of the duodenum, but under the roentgenoscope this can usually be accomplished within five to ten minutes. Once in the duodenum, the balloon is inflated and peristaltic waves then carry it and the attached tube to whatever bowel level is permitted by the period of time allowed and by the length of tubing that is swallowed. Ordinarily it requires about three hours to reach the terminal ileum, and for this bowel level only about 5 feet of the tube need pass beyond the pylorus. The other lumen of the tube, perforated just above the balloon, is available for the aspiration of intestinal contents. The inflated balloon serves also to block the flow of intestinal contents, thus facilitating their complete removal. When desired, an additional small tube is inserted into the stomach for the aspiration of its contents, thus preventing their passage into the duodenum.

To indicate the motility of the intestinal contents, we have noted the time between the introduction of vital red dye into the stomach and its appearance in the intestinal contents, aspirated under a fixed subatmospheric pressure, as well as the actual rate of flow of the intestinal aspirate.

Analyzing the data assembled in this clinic on subjects with normal gastric acidity, we find that the rate of flow of the intestinal contents under fasting conditions was 30 c.c. or less per hour for 17 samples and between 30 and 100 c.c. per hour for 13 samples; in a few it was over 100 c.c. The reaction varied with the part of the intestine from which the specimens were secured, usually being slightly acid when from the duodenum and neutral or alkaline as deeper levels were reached. The duodenal contents averaged a pH of 5.42, the jejunal 6.33, the upper ileal 6.71 and the lower ileal 7.30. It is with these standards that we shall compare our re-

* From the Gastrointestinal Section of the Medical Clinic, University of Pennsylvania Hospital. Read at the Thirty-sixth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 24–27, 1935.

sults in the five special cases, to determine what, if any, consideration should be given the factors of gastric acidity and of gastric motility in interpreting the results of various studies on small intestinal contents.

OBSERVATIONS

In five of the six experiments one or more satisfactory specimens of fasting intestinal contents were obtained as controls (Table 1). These were selected samples because

TABLE I

DATA ON SPECIMENS OBTAINED UNDER FASTING CONDITIONS (CONTROL OBSERVATIONS)

Experiment Number / Subject	Gastric Acidity Free HCl / Total ac.	Distance of Tube beyond Pylorus	Specimen Number	Rate of Flow c.c./hr.	pH
39/Cas.	60/94	30 cm.	1	480	6.45
44/Cap.	83/97	120 cm.	1	264	4.80
19/Dol.	94/124	120 cm.	1	18	7.12
23/Dol.	94/124	150 cm.	1	150	6.88
			2	126	6.70
13/Ros.	Achlorhydria	30 cm.	1	?	6.96
28/Web.	Achlorhydria	150 cm.	1	6	7.13

the flow is intermittent, a period of rapid flow often being followed by one of low rate or by complete cessation for a few moments. After a short period of time, it was usually possible to get an impression as to what samples represented the average rate for each individual. For the hyperchlorhydric cases it varied from 18 to 480 c.c. per hour. Only one satisfactory observation on the fasting rate of flow in an achlorhydric subject was made, and in that case it was very low, 6 c.c. per hour. The reaction of the fasting specimens from each single subject, however, was fairly constant; and for our entire group, whether the samples were from the jejunum or the ileum and whether the gastric acidity was high or absent, the reaction, except in one instance, was practically neutral, from pH 6.45 to 7.13, this being within the range stated for normal subjects. In the one exception, to be referred to later, it was slightly acid.

Let us now consider these experiments separately to show the effects on the intestinal contents of various procedures designed to alter the reaction and motility of the gastric contents. In Experiment 39 (Fig. 1), on a hyperchlorhydric subject with a rapid intestinal motility but a normal reaction, 100 c.c. of a 5 per cent gelatin solution were administered by mouth immediately after securing the control or

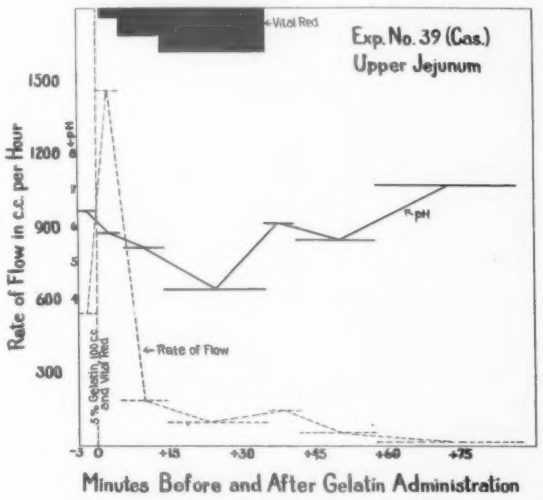

FIG. 1. To indicate variations in the rate of flow and the reaction of the contents of the upper jejunum in a patient with hyperchlorhydria before and after the oral administration of a gelatin solution.

fasting specimen. It was assumed that the additional fluid would, first of all, dilute the fasting gastric contents, so reducing its acid concentration, and that, in addition, its protein content would neutralize some of the acid. This, we know, is what occurs when a protein-containing fluid, such as milk, is introduced into the stomach. In spite of this expectation, when the gastric contents, modified by the gelatin solution, and flowing at an increased rate, first reached the upper jejunum at the 30 cm. level after four minutes, indicated by the appearance of the dye, the reaction of its contents immediately became more acid, dropping from a pH of 6.45 to 5.85. Following that, though the

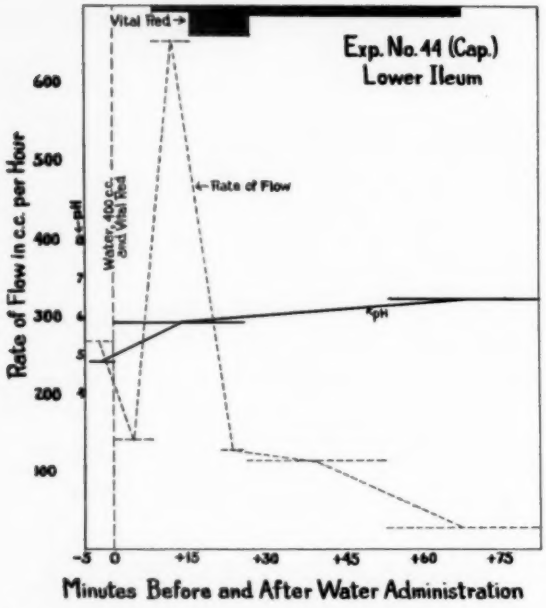

FIG. 2. To indicate variations in the rate of flow and the reaction of the contents of the upper ileum in a patient with hyperchlorhydria before and after the oral administration of water.

motility of the contents was reduced, the reaction continued to fall until after thirteen minutes it was represented by a highly acid secretion and a flow through the duodenum and jejunum that was too rapid for complete neutralization above the 30 cm. level in the jejunum. Later, however, due to the slower output from the stomach or to an increased supply of alkaline fluids in the duodenum, complete neutralization was attained.

In another hyperchlorhydric case (Experiment 44, Fig. 2), with collections from the mid-ileum (120 cm. level), the control specimen showed a relatively acid reaction (pH 4.8), due presumably to chance rapidity of flow from the stomach. After the oral administration of 400 c.c. of water and some vital red, given also with the idea of diluting the acid gastric juice, the modified contents reached the ileum after eight minutes, indicated by the appearance of the dye, and during the interval the rate of flow was not accelerated. Following that period, however, the motility in the intestine was greatly increased, to 666 c.c. per hour, and the reaction was more alkaline, due presumably to a lower concentration of the stomach acid in the large volume of

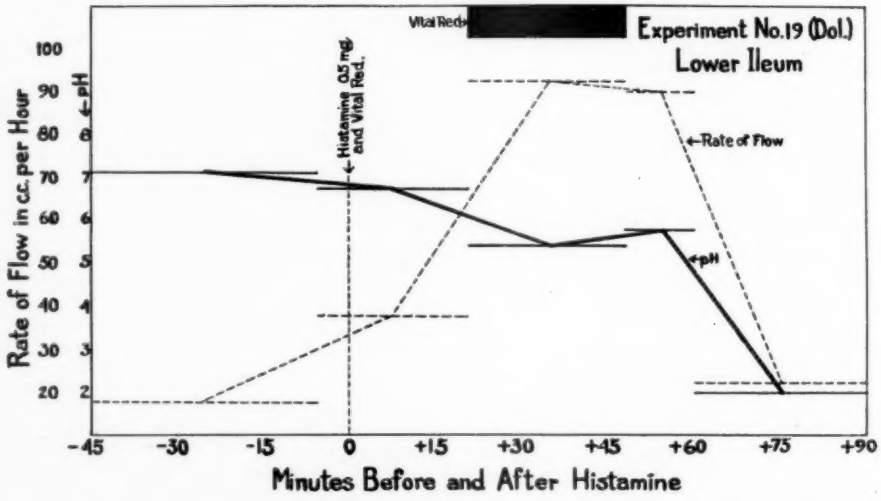

FIG. 3. To indicate variations in the rate of flow and the reaction of the contents of the lower ileum in a patient with hyperchlorhydria before and after the subcutaneous injection of histamine.

pH of 4.28; after thirty-four minutes it had returned to the control level. Thus it seems that the solution caused at once an increased output from the stomach of a fluid. This is made obvious by the finding in the gastric contents at that time of a low chloride concentration (3 milli-equivalents per liter). Subsequently, after all the

diluted gastric contents had passed, the reaction became essentially neutral. This final result seemed to justify the opinion that the original control specimen for some reason did not present the normal fasting reaction; irritation by the tube may have caused complete evacuation of the stomach just before administration of the water.

Two experiments were performed on the third subject with hyperchlorhydria, both after the subcutaneous administration of 0.5 mg. of histamine. They differed in that in the first instance the gastric chyme was allowed to take its normal course through the intestine, whereas in the second it was aspirated continuously while the intestinal collections were being made. The results on the intestinal contents were quite different. In the first (Experiment 19, Fig. 3), it will be noted that the rate of intestinal flow was increased but slightly for the twenty-one minutes before the dye reached the point of collection in the ileum, whereas subsequent to that it was markedly accelerated and at the same time the acidity of the contents increased steadily, finally to a pH of 2.0. In the second (Experiment 23, Fig. 4), in which as much as possible of the gastric contents was removed by continuous aspiration, only a transient increase in flow occurred and the reaction was not appreciably altered. Subsequently the rate of flow was greatly decreased. It may be suggested that the transient increase in flow was due to some influence of the histamine on intestinal secretion, but, working with closed intestinal segments, Abbott has been able to show that this does not occur. It seems more probable, therefore, that the introduction of any substance into the stomach causes reflexly a momentary increase in intestinal peristalsis and motility.

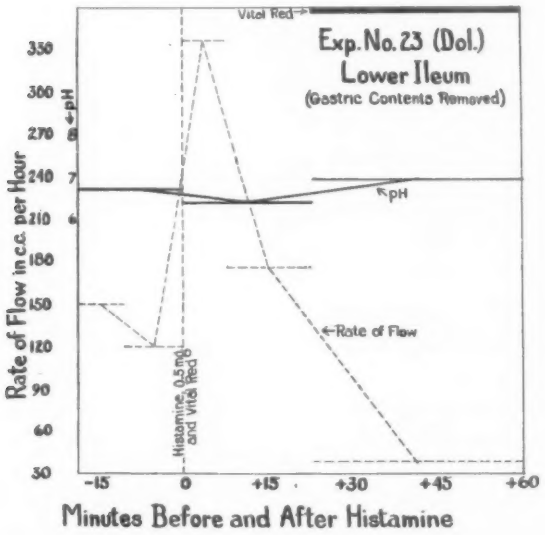

FIG. 4. To indicate variations in the rate of flow and the reaction of the contents of the lower ileum, in the same patient as in Figure 3, before and after the same dose of histamine but while the gastric contents were being aspirated through an additional tube in the stomach.

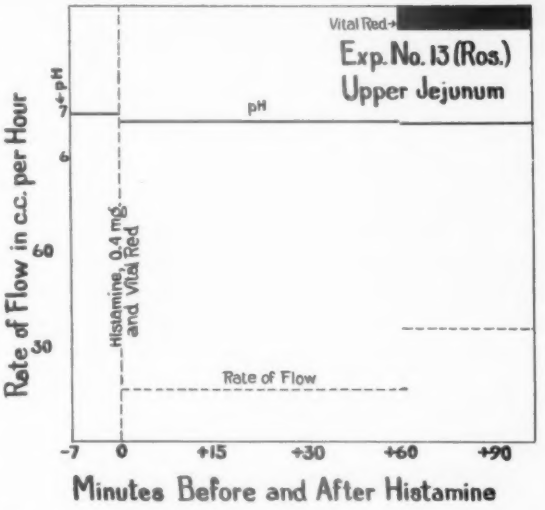

FIG. 5. To indicate variations in the rate of flow and the reaction of the contents of the upper jejunum in a patient with achlorhydria before and after the subcutaneous injection of histamine.

Another experiment (Experiment 13, Fig. 5) was performed to determine the effects of 0.4 mg. of histamine on the reaction and motility of the contents of the upper jejunum in a patient with achlorhydria. The rate of flow was not estimated on the control specimen but it was very low during the 101 minutes after histamine, and the vital red dye, given orally at the same time that the histamine was injected, did not appear for fifty-eight minutes. Neither before nor after that was the reaction of the jejunal contents significantly altered.

In the other achlorhydric patient (Experiment 28, Fig. 6) 50 c.c. of a highly acid solution (with a titration of 160) was administered orally and the collections made from the lower ileum. In this case also the motility was very slow, at least for 170 minutes, as indicated by the rate of flow from the tube and the appearance of the dye, and the reaction was not altered. Finally, after almost three hours, the rate of flow was increased, indicating that the stomach for a time had retained the solution, eventually evacuating its contents, as in the normal individual, after the acidity had been partially neutralized.

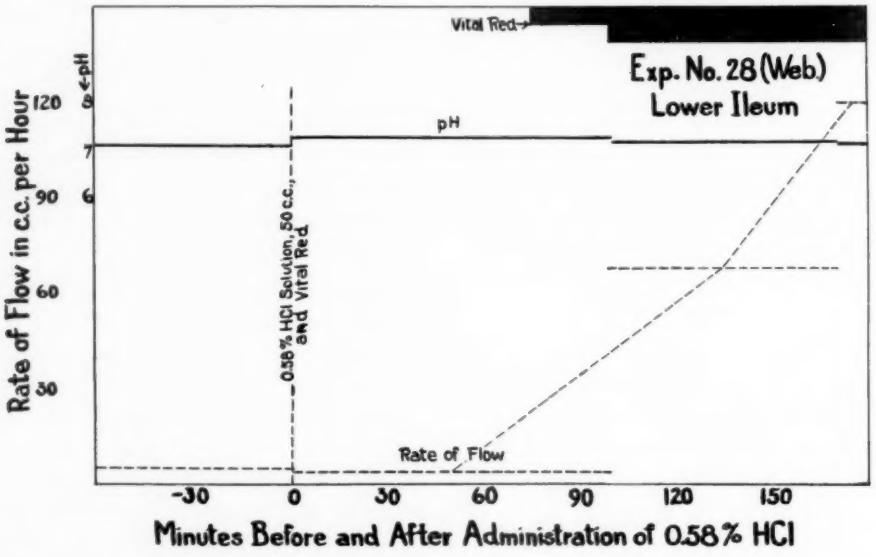

Fig. 6. To indicate variations in the rate of flow and the reaction of the contents of the lower ileum in a patient with achlorhydria before and after the oral administration of a solution of hydrochloric acid.

Discussion

On the basis of these few experiments one hesitates to draw any definite conclusions, but the results obtained by this new method of study seem to justify certain tentative opinions and to suggest further lines of clinical research that may eventually clarify the relationship of the reaction and motility of the gastric contents to the reaction and motility of the intestinal contents.

Marked variation and intermittency in the flow of the intestinal contents has been appreciated since the introduction of roentgenoscopy of the gastrointestinal tract. Not only does the time required for a barium meal to reach the cecum vary with individuals and under different conditions, but also the frequency with which separate masses of barium are passed along from one segment of the bowel to another. We have been able to confirm these observations by our intubation technique,[2,4] which has the advantages of revealing the motility under strictly fasting conditions and of permitting a determination of the chemical reaction of the contents.

We have gained the impression that for each individual, under fasting conditions, a certain more or less fixed rate of intestinal motility exists, and have attempted to indicate this by the selected samples used as controls. This, of course, deserves further investigation.

In spite of the variability of the intestinal motility for different individuals it is to be observed that the reaction of the jejunal and ileal contents under fasting conditions, irrespective of the reaction of the gastric contents, was remarkably uni-

form in our cases, being neutral to slightly alkaline in all but one instance. In that instance, as stated, it seems probable that the control sample was not representative, since subsequent specimens were neutral. These results are in general agreement with those of Mann and Bollman[6] in dogs and of Karr and Abbott[4] in normal human subjects. In both of these publications, however, a number of individual cases with a more acid reaction of the intestinal contents was reported. Our results in cases with hyperacidity, in which for some reason the highly acid gastric contents were rapidly evacuated into the duodenum, suggest a similar explanation for their cases with the more acid reaction. If, however, the acid material in the stomach is slowly evacuated, as apparently occurs under normal conditions and as occurred in our achlorhydric case to which an acid solution was administered, no effect upon the intestinal reaction results.

The effect of histamine deserves special consideration. It will be noted that it had no significant effect on the reaction or the motility of the intestinal contents in an achlorhydria case or in the hyperacidity case in which the gastric contents were aspirated. In the other experiment on the same hyperacidity case it had no decided effect on either function of the intestine until the contents from the stomach itself appeared in the specimens. Thus it seems probable, on the basis of this experiment, that, in man at least, histamine does not directly stimulate secretion below the stomach and that its intestinal effects are dependent entirely upon the action of the drug on the stomach. We do not believe, however, that the acidifying effect of histamine on the intestinal contents is due so much to the increase in gastric acidity as to the increased gastric motility. In other hyperacidity cases no such action has been noted unless a coincident acceleration of motility developed. MacKay[7] showed in animals that after the intravenous injection of histamine there occurs first a contraction of the intestine, then a relaxation and finally an increase of tonus and peristalsis. We have observed roentgenoscopically in the barium filled human stomach, after the subcutaneous injection of histamine, a similar transient contraction of the duodenum, followed by an increase of gastric and intestinal peristalsis and of gastric emptying. Furthermore, our Experiment 44 shows clearly a delayed but decided increase in the flow of the intestinal contents after histamine.

TENTATIVE CONCLUSIONS

(1) The jejunal and ileal contents of man, under fasting conditions and irrespective of the reaction of the gastric contents, tend to maintain a relatively neutral reaction.

(2) The neutral reaction is maintained so long as gastric motility is low, but when, in the hyperacid case, the gastric motility is increased, after histamine or the oral administration of a protein solution, a more acid intestinal reaction results.*

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* For discussion see page 315.

THE EFFECT OF FOODSTUFFS ON THE EMPTYING OF THE NORMAL AND OPERATED STOMACH AND THE SMALL INTESTINAL PATTERN*

By I. S. RAVDIN, M.D., E. P. PENDERGRASS, M.D., C. G. JOHNSTON, M.D., *and* P. J. HODES, M.D.
PHILADELPHIA, PENNSYLVANIA

FROM the early part of the last century when William Beaumont made his historic observations on Alexis St. Martin, the study of gastric physiology has occupied a prominent place in American laboratories. Beaumont insisted and proved that water disappeared rapidly through the pylorus. He supplied the first comprehensive and thorough study of the motions of the stomach, and he provided ample evidence of the digestibility in the stomach of different articles of the diet.

It was not, however, until Roentgen gave us an additional method of studying the gastrointestinal tract that many of the aspects of the motor functions of this tract could be studied under physiological conditions. The observations of Cannon,[2] Carlson,[3] Ivy,[8] Hedblom and Cannon[7], Quigley, Zettelman and Ivy,[10] Alvarez,[1] and a host of others, have added valuable information to our knowledge of gastric emptying, but as yet many of the important considerations of the subject must await further investigation.

In the last decade of the 19th century London convincingly demonstrated that fatty foods retarded the gastric emptying, a fact which Beaumont had observed in the early part of that century. Cannon amplified Beaumont's observations that the emptying time of the stomach varied greatly when different foods were placed in it. With Hedblom[7] he showed that the consistency of the ingested food was an important factor in emptying time. Carnot and Chassevant[4] demonstrated that hypertonic solutions of salt and sugar remained in the stomach for a considerable period. More recently Gianturco[6] has studied the effect of a wide variety of foodstuffs on the gastric emptying time of the cat. He has substantiated many of the earlier observations and added important data to our knowledge of this subject. He concluded that "the emptying time of different foodstuffs depends first on the physical condition, consistence, size of the particles and so forth, and second, on the chemical nature of the substance."

Our interest in this important subject arose several years ago following studies on the absorption of glucose from loops of the small intestine. We concluded that the rate of absorption of glucose from such loops was dependent in large part upon the concentration and the volume of the solution used. With increasing concentrations increasing amounts of glucose were absorbed. With increasing volumes of the same concentration increasing amounts of glucose were absorbed (Tables I, II, and III). These observations were not in agreement with the observations of Cori[5] who had concluded that the amount of glucose absorbed from the intestinal tract had no relation to the concentration of the solution used, since he had found that, regardless of concentration, the amount of glucose absorbed in a given time depended solely upon the body weight.

It occurred to us that the difference in the results obtained by Cori and by ourselves lay in the fact that Cori placed his solutions in the stomach, thereby using the gastrointestinal tract as a physiological unit, while we had used only a segment of the unit. Because of this difference we investigated the changes in the concentration of various solutions of glucose when placed

* From the Laboratory of Surgical Research School of Medicine, University of Pennsylvania, and the Departments of Roentgenology and Surgery of the Hospital of the University of Pennsylvania, Philadelphia. Aided by a grant from the Faculty Research Committee. Read at the Thirty-Sixth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 24–27, 1935.

TABLE I

THE EFFECT OF VOLUME OF THE SOLUTION AND AMOUNT OF GLUCOSE ON THE RATE OF ABSORPTION. DOG NO. 941

Date	Time	Volume in	Volume out	Conc. in	Conc. out	Total in	Total out	Total lost
	hr.	c.c.	c.c.	gm./100c.c.	gm./100c.c.	mg.	mg.	mg.
7-5-32	¼	20	16.0	2.6	1.6	520	256	264
	¼	40	23.5	2.6	1.9	1,040	447	593
	¼	20	10.0	2.6	2.4	520	240	280
7-8-32	¼	10	38.0	30.6	6.0	3,060	2,275	785
	¼	20	60.0	30.6	8.0	6,120	4,825	1,295
	¼	30	67.0	30.6	11.0	9,180	7,350	1,830
	¼	40	76.0	30.6	13.2	12,240	10,000	2,240

TABLE II

THE EFFECT OF CONCENTRATION ON THE ABSORPTION OF GLUCOSE. DOG NO. 941

Date	Time	Volume in	Volume out	Conc. in	Conc. out	Total in	Total out	Total lost
	hr.	c.c.	c.c.	gm./100c.c.	gm./100c.c.	mg.	mg.	mg.
6-29-32	¼	20	25	2.5	0.98	500	245	255
	¼	20	50	13.3	4.2	2,660	2,075	585
	¼	20	56	29.0	7.9	5,800	4,450	1,350
7-19-32	¼	20	35	34.2	16.0	6,840	5,620	1,220
	¼	20	51.5	55.0	15.9	11,000	8,200	2,800
7-25-32	¼	20	19.5	2.2	0.76	440	148	292
	¼	20	41.0	10.0	3.6	2,000	1,470	530
	¼	20	59.0	22.0	5.2	4,400	3,050	1,350

TABLE III

THE EFFECT OF VARYING VOLUME AND CONCENTRATION ON THE ABSORPTION OF GLUCOSE. DOG NO. 941

Date	Time	Volume in	Volume out	Conc. in	Conc. out	Total in	Total out	Total lost
	hr.	c.c.	c.c.	gm./100c.c.	gm./100c.c.	mg.	mg.	mg.
7-6-32	¼	20	20.0	5.3	3.2	1,060	646	414
	¼	20	18.3	10.2	3.8	1,020	690	330
7-11-32	¼	20	18.5	5.4	3.2	1,080	592	488
	¼	15	19.0	7.9	2.9	1,185	741	444
7-12-32	¼	30	8.5	1.4	1.2	420	102	318
	¼	18	6.0	2.7	2.2	405	132	273

in the stomach of the unanesthetized dog. The concentration of the solutions used varied from 3.5 to 50 per cent. At the end of one hour fluid was removed from the stomach and various segments of the small intestine. The concentrations found in the small bowel one hour after the introduction of a wide range of concentrations in the

stomach were of such an order that had these been placed in the isolated small intestinal loop no difference in the rate of absorption would have been demonstrable (Table IV).

TABLE IV

CHANGES IN THE CONCENTRATION OF GLUCOSE

Dog	Time	Concentration Glucose in (Stomach)	Concentration Glucose out (Stomach)	Concentration Glucose out (Small Intestine)
No.	hr.	gm. per cent	gm. per cent	gm. per cent
762	1	3.5	2.3	—
793	1	10.4	6.3	3.5
788	1	14.9	7.4	3.3
766	1	20.0	5.0	2.6
794	1	27.0	10.8	3.6
809	1	50.0	17.9	5.3

The investigations provided evidence on the important part which the stomach and duodenum normally play in preparing certain of our foodstuffs for acceptance by the small intestine. It has been suggested by Shay and Gershon-Cohen[11] that the control of gastric emptying is due to the activity of the pylorus reacting to stimulation of the duodenal mucosa. While Shay and Gershon-Cohen's observations were carried out on human subjects using roentgenoscopic observation of a barium mixture as a means of determining the rate of emptying of the stomach, our experiments were made on dogs using an entirely different criterion for the determination of the emptying of the gastric contents.

If the pyloric sphincter were the sole factor in preventing the passage from the stomach of substances not acceptable to the duodenum, gastroenterostomy, the Billroth I, or Pólya operation should permit the rapid passage into the small intestine of substances, which, under normal conditions, this portion of the intestinal tract is not called upon to accommodate. The concept of such procedures as "dumping operations" is one that is widely accepted and generally taught.

In a series of dogs in which the three operative procedures had been carried out, we determined that, regardless of the type of operation, the stomach functioned normally, in that the gastric residue at the end of one hour was considerable, and well within the limits of the amount we would expect to find in the unoperated dog. Furthermore, the concentrations of glucose in the small intestine one hour after their introduction into the stomach were again found to be at or near isotonicity (Chart I). We could only conclude that any restraining influence was due to changes in the activity of the gastric wall or to contraction of the small intestine below the stoma. Our impression was further strengthened by the data of Gianturco[6] who found that the emptying time, as determined roent-

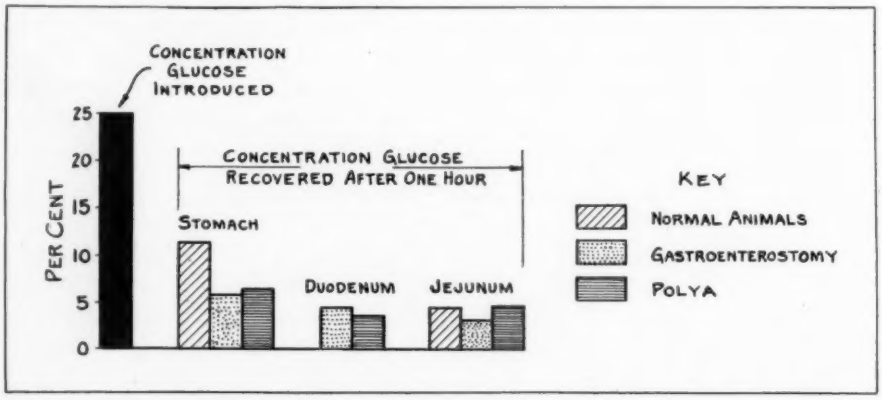

CHART I

genographically, of the unoperated and operated cat was approximately the same.

These investigations which at first sight may appear widely divergent, but which on closer observation are intimately associated, led us to investigate the effect of alterations of the standard barium meal on the normal gastric emptying time and after various gastric operations.

We have studied the effect on the gastric emptying time of a wide variety of substances when added to a standard amount of barium sulphate—5 ounces. We have adopted a standard meal of 5 ounces of barium sulphate and 3 ounces of water because this meal is of such consistency as to give excellent gastric visualization and at the same time provide for adequate study of the small intestine. At this time we wish to report on only a few of these substances. The studies have been made in both dog and man.

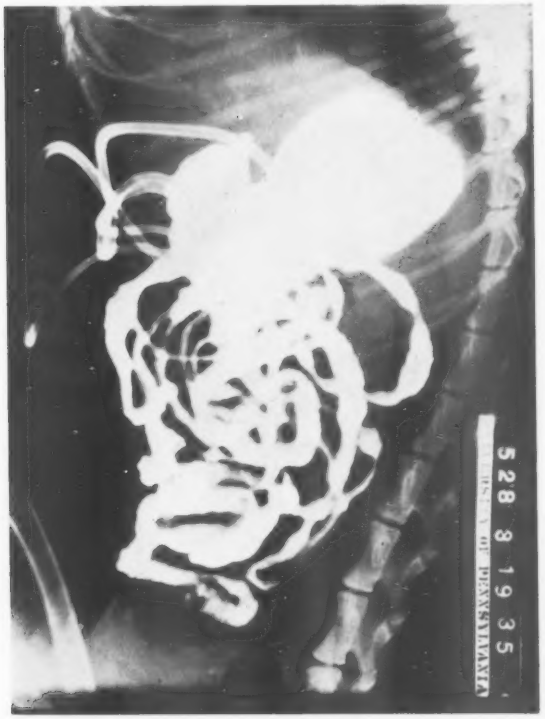

Fig. 1. Double intubation of the common bile duct —water-barium meal. Nothing was introduced through the common duct tube during the period of study. The film was made one hour and twenty minutes after the introduction of the water-barium meal in the stomach. The small intestines are filled with barium.

Fig. 2. Double intubation of the common bile duct —water-barium meal. Olive oil was dripped into the duodenum through the common duct tube at the rate of 1 c.c. per minute. One hour after introduction of the meal none of the barium had left the stomach.

In the dog we have verified previous observations by others that the addition of 50 per cent glucose or of a small amount of olive oil to the barium produced a marked delay in the gastric emptying. It was also determined that when olive oil or a hypertonic solution of glucose was dripped in the duodenum through a tube in the common bile duct during the period of observation, gastric emptying was nearly completely stopped during the period of duodenal instillation. The effect of solutions containing proteins was, however, not nearly so great since although the emptying time was delayed over the normal it was not so dramatically stopped (Figs. 1, 2 and 3).

Quigley et al[10] have postulated that the

FIG. 3. Double intubation of the common bile duct —water-barium meal. A 50 per cent solution of glucose was dripped into the duodenum at the rate of 1 c.c. per minute. One hour later none of the barium had left the stomach.

effect of certain of the foodstuffs on the gastric emptying time is the result of a humoral, hormonal mechanism. The opportunity arose of testing this hypothesis by placing olive oil and hypertonic glucose solution in a modified Thiry loop of the jejunum while the gastric emptying time, after a barium meal, was being observed. It might be expected that if the retardation of the gastric emptying time was the result of a hormonal mechanism these substances should have proved to be equally as efficacious as when placed in the duodenum. We were, however, unable to demonstrate any effect on the emptying time of the stomach when these substances were placed in the isolated high jejunal loop. If a hormonal mechanism exists it is not effective in the isolated upper jejunum (Figs. 4, 5 and 6).

In man we wish to report the results obtained when certain variations of the standard barium meal were used. The addition of hypertonic glucose solutions, olive oil and protein solutions in such amounts as not greatly to vary the consistency of the meal, delayed the gastric emptying time in every instance, glucose and oil being the most effective. We also tried what we have termed an ideal barium meal which consisted of 5 ounces of barium sulphate, 40 grams of carbohydrate, 30 grams of protein and 28 grams of olive oil. The consistency of the mixture was not unlike the consistency of the other meals. This meal likewise delayed the gastric emptying.

The small intestinal pattern varied greatly with the various types of meals. In the water-barium meal the small intestinal contents progressed as a continuous stream showing various patterns throughout the jejunum and ileum. After the glucose-barium meal the small intestinal stream was of an intermittent type, the

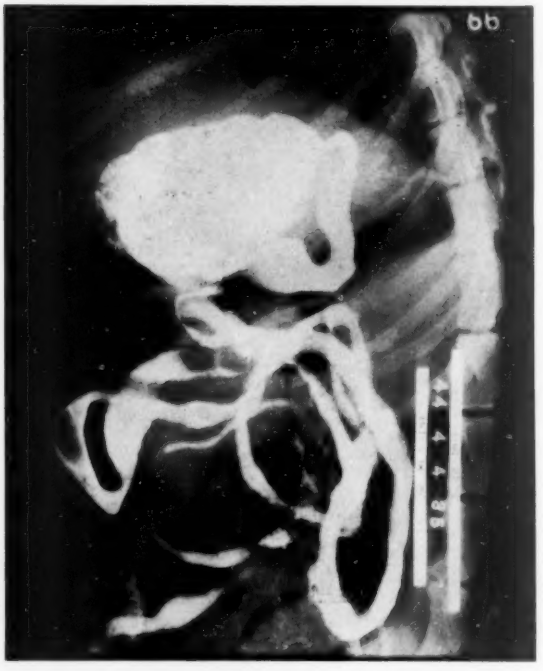

FIG. 4. Jejunal loop—water-barium meal. During the period of study no solutions were placed in the jejunal loop. The barium promptly began to leave the stomach, the film being made ten minutes after the introduction of the barium.

pattern of a very much coarser arrangement than with the water-barium meal. The small intestinal stream after the oil-barium meal was of a smudged intermittent appearance and the intestinal pattern of a very heterogeneous type. In the protein-barium meal alone was the small intestinal pattern in any manner similar to that observed after the water-barium meal (Figs. 7, 8, 9 and 10).

It is of interest to us as clinicians to determine the effect of various foodstuffs on the gastric emptying time of the patient who has undergone a gastric operation resulting in a new stoma. We have examined a series of patients at intervals after posterior gastroenterostomy, the Billroth II and the Pólya operation.

We plan to report our observations at some length later, but we wish to say at this time that regardless of the type of meal which the roentgenologist used, the stomach recently operated upon does not function as it will four to six weeks after operation. Kirklin[9] has called attention to this fact but it is not generally recognized by roentgenologists, and failure to appreciate the significance of the roentgen findings has led to many unnecessary operations for an obstruction, the result of a supposed defect in the operative technique. Any decision as to subsequent operative procedures must depend upon the clinical findings although the roentgen examination may be suggestive if carried on for a period of twenty-four to forty-eight hours. In other words, at six hours little or no contents may have passed out of the stomach but at the end of twenty-four to forty-eight hours there may be a relatively large amount in the colon (see Fig. 11) even though there is still a tremendous residue in the stomach. If, on the other hand, there is an obstruction, no contents may

Fig. 5. Jejunal loop—water-barium meal. During the period of observation 50 per cent glucose was dripped into the jejunal loop at the rate of 1 c.c. per minute. This film was made ten minutes after the introduction of the water-barium meal and shows prompt emptying of the stomach.

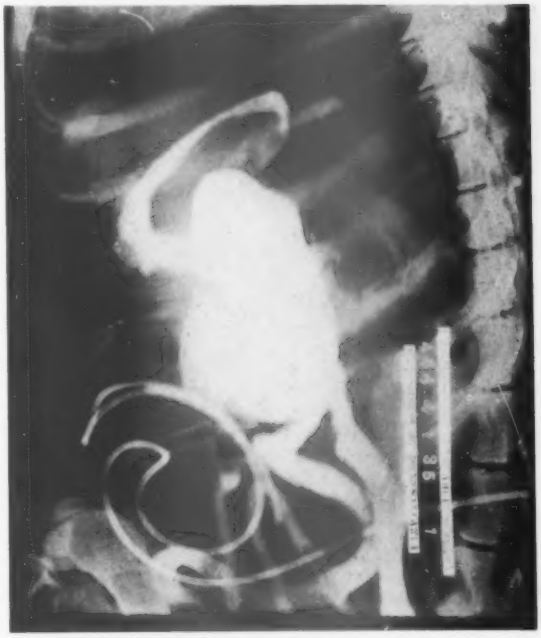

Fig. 6. Jejunal loop—water-barium meal. Olive oil was dripped into the jejunal loop at the rate of 1 c.c. per minute during the period of study. This film was made ten minutes after the introduction of the water-barium meal and shows prompt emptying of the stomach.

FIG. 7. Adult human—water-barium meal. The intestinal pattern is of the type obtained in a normal individual when the standard water-barium meal is given.

FIG. 8. Adult human—water-barium meal. The same individual with 2 ounces of 50 per cent glucose mixed with the barium. Note the difference in the intestinal pattern.

FIG. 9. Adult human. This roentgenogram shows a normal adult human after introduction of a standard barium meal to which 1 ounce of olive oil has been added.

FIG. 10. Adult human. This roentgenogram shows a normal adult human after introduction of a standard barium meal to which protein has been added.

Fig. 11. Adult human. Seventeen days after a Pólya operation; the stomach is greatly dilated. This roentgenogram was made twenty hours after the introduction of a water-barium meal and shows nearly complete gastric retention.

Fig. 12. Adult human—water-barium meal. Three months after a Pólya operation the stomach is emptying normally.

Fig. 13. Adult human. Three months after a Pólya operation (same patient). A 50 per cent solution of glucose is mixed with the water-barium meal. Note the delay in gastric emptying and the change in the small intestinal pattern.

Fig. 14. Adult human. Three months after a Pólya operation. Olive oil has been added to the water-barium meal and even though the pylorus is not present the gastric emptying has been stopped.

pass beyond the point of obstruction in twenty-four to forty-eight hours.

The effect of olive oil, protein and hypertonic solutions of glucose when added to the barium meal was essentially the same in the patients who had been operated on as in the unoperated subjects, and the small intestinal patterns were similar to those previously described. In no way did the new stoma provide for immediate emptying into the jejunal segment even when a simple water-barium meal was used. It must therefore be concluded that the common impression that the new stoma provides for immediate gastric evacuation is not correct under the conditions of feeding to which the stomach is normally subjected. Under such conditions the gastric emptying is indeed similar to that observed with the pylorus intact (Figs. 12, 13 and 14).

DISCUSSION

The data collected by many investigators provide adequate evidence that even in individuals with a normally functioning gastrointestinal tract the progress of a meal is profoundly influenced by the composition of the meal. Not only is the progress of the meal influenced but the small intestinal pattern may vary widely with a variation in the type of meal which is administered.

As far as we can determine at the present time, a mixture of water and barium exerts no specific influence on the gastric emptying time and should therefore be adopted as the standard meal for the determination of pathological lesions of the gastrointestinal tract. We suggest that the barium-water meal we have adopted is a most satisfactory one. Since the emptying time of the stomach will vary if the meal is made up in any vehicle other than water the widespread variety of vehicles now in use should be discouraged. It is not possible to give satisfactory impressions of the emptying time or the small intestinal pattern in the course of clinical study of a patient when the study is made at one time with a water-barium meal and at another with a malted milk-barium meal.

It is of the greatest importance that roentgenologists familiarize themselves with the small intestinal patterns obtained under the conditions of variations of the vehicle of the barium meal. The great importance which the clinician now attaches to the roentgen study of the small intestine necessitates a more active interest of roentgenologists in this tract and in the variations which various foodstuffs may produce in the pattern of a normal tract.

The alterations of the gastric emptying time produced by various foodstuffs open a new field for roentgenographic exploration. It is to be hoped that in the future roentgenologists will study various functional disturbances of the gastrointestinal tract, which are associated with dyspepsia, with a meal similar to that which we have termed the ideal meal or some variation of it. It is of importance that the clinician be able to obtain information of the motor function of this tract under the conditions which are daily imposed upon it. From this point of view the field of roentgenographic study of gastrointestinal disorders will become widely extended in much the same manner as the field of allergy has been enlarged by our knowledge of individual food tolerance.

And finally, we wish to emphasize the necessity of caution on the part of the roentgenologist in interpreting the results obtained by roentgen study of the stomach after a recent operation upon it. The disturbances in emptying which occur after operation are frequently of a complicated character and we do not believe it possible for the roentgenologist to determine whether or not the failure to empty is amenable to further surgical interference.

The data which we have accumulated on the stomach after operation on dog and man lead us to the conclusion that under the conditions normally imposed on the stomach by diet, the stomach after operation functions as does the normal stomach with the pylorus intact. Under such con-

ditions the new stoma, regardless of size, does not in itself permit of rapid gastric emptying.

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DISCUSSION OF SYMPOSIUM ON RESEARCH WORK ON THE SMALL INTESTINES*

HARRY M. WEBER, Rochester, Minn. I am not at all certain that I personally have fully grasped the entire significance of the work which has just been presented. However, I am very favorably impressed with every part of it, and particularly with its fundamental quality. It is a fine demonstration of the fruitful results to be obtained when all departments interested in gastroenterologic problems will cooperate. Many ideas worthy of discussion have suggested themselves, but I wish to confine my remarks to that phase of the work which has to do with the roentgenologic morphology of the small intestine.

I have always had an idea that the motility of the gastrointestinal tract could hardly be judged fairly using a contrast material of the physical and chemical nature of barium sulphate. Its high specific gravity, its coarse texture, its tendency to accumulate in dense, clumped masses, especially with dehydration of the suspending fluid, all seemed to me to vary too greatly from the physical properties of the materials which the intestinal tract is designed to handle. The experiments just described show that the physical and chemical nature of the suspending substance has at least as great an influence on the motility and on the character of the mucosal relief patterns of the small intestine as has the material suspended, and they will serve as a reminder to use great caution in interpreting the very complicated mucosal relief patterns of the small intestine, influenced as they are by many other factors besides pathologic processes and the materials in contact with the mucosal surface. Not the least important of these are the emotional or psychic disturbances which the subject might, and probably is, undergoing at the very time and because of the investigation.

The authors remind us that this is only the beginning of their work. They have presented a method, and with the development of the double- and triple-lumen tube, an instrument to facilitate further investigation along the same lines. By following their lead, by taking their very well-placed advice about adopting a standard set of conditions for the roentgenologic investigation of the small intestine, and by devoting to this problem the same diligent cultivation already given to the stomach and large intestine, the diagnostic efficiency of roentgenologic methods applied to the small intestine will eventually be raised to the same high plane already achieved for the segments of the gastrointestinal tract proximal and distal to it.

* Papers by Abbott and Pendergrass, Miller and Karr, and Ravdin, Pendergrass, Johnston and Hodes.

OBSERVATIONS ON SMALL INTESTINAL PHYSIOLOGY IN THE PRESENCE OF CALCIFIED MESENTERIC LYMPH NODES*

By ROSS GOLDEN, M.D.
NEW YORK CITY

THE association of abdominal pain with tuberculous mesenteric lymphadenitis has long been known (Bier, 1892). For many years the diagnosis was made only after exploratory operation. Corner, in 1905, reported the first case in which a dense shadow on a roentgenogram was proved to be a caseo-calcareous lymph node and emphasized the importance of the roentgen method of detecting this disease. In 1908 he reported that this patient remained free from symptoms four years after removal of the node and again stressed the help to be obtained from a roentgenogram of the abdomen. During the succeeding years numerous case reports by surgeons brought out the puzzling character of the symptoms and the difficulty of differential diagnosis; the condition was called "primary" or "surgical" tuberculosis of the abdominal lymph nodes and the frequency with which it simulated appendicitis was noted. Yet two decades passed after Corner's original report before discussions of the importance of roentgenograms of the abdomen in the diagnosis of this disease began to appear in the literature (Dunham and Smythe, 1926; Golden and Reeves, 1929; Auchincloss, 1930). In his excellent monograph, Strömbeck (1932) presents an exhaustive discussion of mesenteric lymphadenitis and a review of the literature. A recapitulation of various points such as incidence, mechanism of infection, pathology of the disease, its clinical vagaries, etc., will not be attempted here.

The symptoms of mesenteric lymphadenitis may simulate many other abdominal conditions. The pain may vary from a dull grumbling discomfort, usually in the right lower quadrant, to attacks so violent that surgical intervention may be considered or even done. The mechanism by which this pain is produced in uncomplicated cases has never been explained. Inflammatory irritation of the peritoneum over the node, and mechanical irritation of the nerve fibers in the mesentery with disturbed visceral physiology have been suggested (Golden and Reeves). Evidence of the former is usually lacking at operation. The possibility of the latter is suggested by the colicky character of the pain in some cases, together with absence of disease of the intestine itself. A solidly calcified node seems to be just as capable of causing symptoms as one in which the disease is active. The purpose of this paper is to present certain observations in 7 cases in which various disturbances in the physiology of the small intestine appear to have been directly associated with calcified mesenteric lymph nodes.

METHODS

In one of the 7 patients, the evidence of disturbed physiology in the small intestine was noted during operation; in the others it was obtained by roentgen observations following the ingestion of barium. To examine the small intestine it is now our custom to give the patient, on an empty stomach, a quantity of barium suspension not to exceed 4 ounces in volume and to take films of the abdomen at intervals of half an hour, sometimes of fifteen minutes, until the barium has entered the large intestine and the terminal ileum has been satisfactorily seen. The patient lies prone and the exposure time is one-tenth of a

* From the Department of Radiology of the Presbyterian Hospital and of the College of Physicians and Surgeons of Columbia University, New York. Read at the Thirty-sixth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 24–27, 1935.

second. Two or three roentgenoscopic observations are usually made. The patient takes his midday meal as usual. Six, nine, and twenty-four hour films complete the examination. This procedure has come to be known in our department as a "small intestine study," and was used in most of the cases discussed below.

NORMAL SMALL INTESTINAL PHYSIOLOGY

Under the usual normal conditions, a small intestine study shows that the stomach empties continuously and barium passes steadily in a caudad direction, reaching the cecum in one and a half to four hours. Although peristaltic movements do not take place continuously, each successive film shows progress distally in the position of the head of the barium column. These peristaltic movements appear as smoothly flowing narrow constrictions passing in a caudad direction; behind the constriction the wall relaxes promptly and assumes its normal width. The segmental "pendulum" movements are likewise followed by prompt flexible relaxation of the wall. If there is no delay in the stomach, the ileum should be empty in nine hours. The barium mass in the normal small intestine is usually continuous, that is, not broken up into separate small oval boluses. The width of normal, barium-filled loops varies from 1.5 to 3.0 cm., and is usually 2.0 to 2.5 cm.

CASE REPORTS

Case I (Unit No. 255148). A girl, aged seventeen, went to Dr. Hugh Auchincloss April 4, 1925, because of asymmetrical breast development. A history of nausea and indefinite abdominal symptoms of five years' duration led Dr. Auchincloss to suspect the possibility of calcified nodes. A film of the abdomen April 6, 1925, disclosed a group of calcified nodes overlying the 5th lumbar vertebra. The abdominal discomfort continued. Another film five years later (Jan. 9, 1930) showed no change in the shadow of the nodes. On Jan. 13, 1930, the patient was examined with the roentgenoscope six hours after the ingestion of barium, when the ileum, cecum and ascending colon were filled. The calcified nodes were only slightly movable and were definitely tender on pressure. One loop of ileum was pulled up close to these nodes and moved only as much as the nodes, while other ileal loops could be pushed around freely. This limited loop was narrower than the others and tended to close off and remain in a state of spasm for some time after a peristaltic wave passed over it. This was in interesting contrast to the normal peristalitic activity of the ileum elsewhere. At nine hours barium remained in the terminal ileum. At operation on May 10, 1930, two large masses of partially calcified, cheesy, old tuberculous nodes were found in the mesentery halfway between its root and the intestinal margin, and intimately associated with mesenteric arteries and veins. The mesentery was scarred, puckered up and considerably shortened. The nodes were dissected out with great difficulty. Convalescence was uneventful. Three months later she had abdominal cramps occasionally for two weeks ending with severe abdominal pain suggesting intestinal obstruction. After a vomiting attack lasting fifteen minutes the pain suddenly stopped. A small intestinal study Aug. 19, 1930, disclosed no evidence of the abnormal peristalsis and spasm noted at the first examination and no nine hour ileal residue.

Case II (Unit No. 60921). A woman, aged thirty-one, was admitted to the hospital in 1924 because of attacks of swelling of the abdomen of ten years' duration, sometimes associated with abdominal pain and vomiting and rarely with fever. Some of the attacks were so violent as to suggest intestinal obstruction. A calcified mesenteric lymph node was first demonstrated in 1923. A gastrointestinal examination done in the usual way in 1924 disclosed delay of barium in the ileum at six hours with considerable gas in the small intestine and a twenty-four hour ileal residue. No satisfactory explanation of the symptoms was found, and they continued. A small intestinal study Jan. 3, 1929, when the abdomen was markedly distended, disclosed a delay of more than three-quarters of an hour of the head of the barium column in the upper ileum at the site of the calcified node. No nine hour ileal residue was found. A re-examination April 3, 1929, when the abdomen was flat, disclosed no delay at the site of the node. It seemed hardly possible that the node could be responsible for the attacks of abdominal distention. Her psychic background

Fig. 1. Case II. The head of the barium column stopped for over three-quarters of an hour in the lower jejunum at the level of the calcified node, the shadow of which overlies the iliac crest.

was very bad and pseudocyesis seemed to be the most likely diagnosis.

Case III. A man, aged twenty-four, went to his physician because of abdominal pain. His appendix was removed when he was eighteen years old. A year later he began to have attacks of generalized abdominal discomfort without relation to meals, aggravated by stress and increased activity. At the age of twenty-one, the attacks began to be associated with diarrhea, 4 to 5 stools a day. Rest and heliotherapy seemed to cause some improvement and then the symptoms recurred. Later under a low residue, high calorie diet he failed to gain weight. A film of the abdomen disclosed a large mass of calcified, tender lymph nodes overlying the right margin of the 4th and 5th lumbar bodies. The usual gastrointestinal examination April 9, 1931, disclosed a 50 per cent six hour gastric residue and a twenty-four hour residue in the terminal ileum. A small intestinal study, April 19, 1932, showed a delay of the head of the barium column for over two hours in the terminal loop of ileum at the site of the calcified lymph nodes. A second small intestinal study, Nov. 25, 1932, disclosed even more strikingly the same delay of over two hours of the head of the barium column in the terminal ileum, with spasm in the loop immediately adjacent to the nodes. At the roentgenoscopic examination, when this loop was touched, it went into spasm and expelled barium in both cephalad and caudad directions. The mobility of this loop and of the node were equally limited. The distance between the calcified nodes and the adjacent ileum could not be increased, but the two shadows could be approximated. Pushing the nodes to the left caused the intestine to be displaced in the same direction. A dietary and hygienic regimen plus the efforts of a Christian Science mother produced enough improvement so that operation in this case was indefinitely deferred.

Case IV. (Unit No. 326831). A nurse, aged twenty, had a series of attacks of cramp-like epigastric and para-umbilical pain accompanied by nausea and anorexia. There were no other signs or symptoms. The attack for which she was admitted had lasted two weeks. Films of the abdomen showed a calcified node sometimes on the left and sometimes on the right of

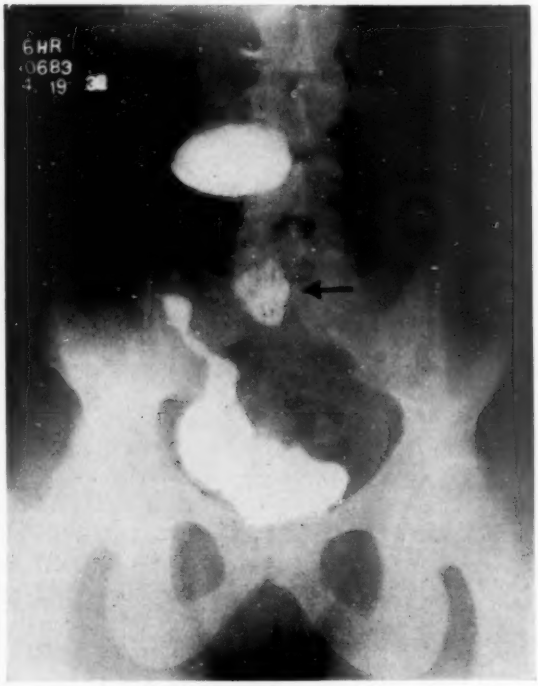

Fig. 2. Case III. The arrow points to a group of calcified lymph nodes. The head of the barium column in the terminal ileum did not move for over two hours at two examinations seven months apart. The spasm of the terminal ileum is clearly shown. A six hour gastric residue is present.

the lumbar spine, indicating that it lay well out in freely movable mesentery. The usual small intestinal study for some reason was not done. Roentgenoscopic inspection of the abdomen two and four hours after a barium meal showed that the opaque material had passed below the loop adjacent to the calcified node; in four hours the stomach still contained about a third of the barium and the head of the opaque column had reached the descending colon. Hypermotility was apparently present in the upper part of the small intestine and in the large intestine, and because of the former no localized disturbance in the loop adjoining the calcified node could be demonstrated. Operation Jan 14, 1932, under avertin anesthesia, disclosed a group of calcified nodes in the mesentery of the lower jejunum about halfway between the root and the periphery. The loop of intestine adjacent to them was somewhat dilated for a distance of 30 cm. During the operation peristalsis was quite active and it was noted that contraction waves were definitely slowed up when they reached the loop adjacent to the nodes. The peritoneum over them was puckered and contracted. No evidence of peritoneal tuberculosis was observed. With considerable difficulty, because of involved blood vessels, the group of nodes was dissected out. The section of intestine about 5 cm. in length adjacent to the nodes became somewhat cyanotic and the question arose as to whether its blood supply had been impaired. The surgeons finally decided that its viability had not been compromised. The nodes were found to be shells of fibrous tissue enclosing calcified masses After three days of postoperative pain, she became symptom-free. About a month later, however, she began to have cramping pain on the left side of the abdomen, induced by eating. A small intestinal study disclosed a narrowed irregular area in the lower jejunum, which at times was seen to expand as barium was forced through. Under the stimulus of palpation, powerful reversed peristaltic waves drove the barium in a cephalad direction. This loop was definitely limited in mobility. Barium still remained proximal to the narrowed area at nine hours. The second operation, March 31, 1932, disclosed a constriction in the small intestine about 2.5 cm. in length with marked thickening of the wall. Immediately adjacent to it was a large uncalcified lymph node. Many small elevated nodules varying in size up to 2.5 mm., resembling tubercles, were scattered over the visceral peritoneum. They were not present at the first operation. The narrowed loop of intestine was resected. The constricted area was found to contain a small ulcer with a dirty necrotic slough. On histologic examination the ulcerated area was heavily infiltrated with round cells, plasma cells and neutrophiles; destruction of the muscularis mucosae and, in one place, of the circular muscle was noted. The enlarged lymph node showed evidence of chronic lymphadenitis and guinea pig inoculation proved negative for tuberculosis. Recovery was uneventful and the patient has remained symptom-free. It was thought that the constriction of the intestine was the result of impaired circulation. However, that explanation does not seem to suffice for the small tubercle-like nodules noted on the peritoneum at the second operation. Similar structures have been described in the condition called ileitis (regional ileitis) and seem to be a manifestation of some sort of infection.

FIG. 3. Case IV. At operation under avertin anesthesia the surgeon observed a definite slowing up of peristaltic waves in the segment of ileum adjacent to the calcified nodes, and, in moments of relaxation, this segment was larger than those above and below it.

CASE V. A man, aged twenty-nine, went to his physician because of pain in the right side of the abdomen. The first attack, six years

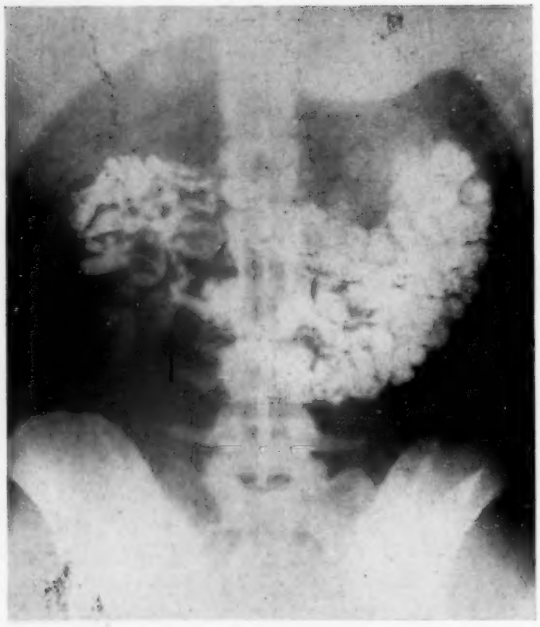

Fig. 4. Case vi. A twenty-two year old nurse had a long series of attacks of abdominal pain unrelieved by appendectomy. Progression of barium through the ileum was delayed for over an hour at the level of the calcified nodes (arrows). Spasm, manifested on the film by long narrow areas, and abnormal overactive peristalsis were observed roentgenoscopically in the loops adjacent to the nodes.

previously, was associated with blood in the urine and was thought to be due to a ureteral stone. Cystoscopy disclosed a kinked ureter which the procedure was supposed to have cured. The attacks of dull or stabbing pain in the right flank radiating to the back recurred with increasing frequency, often induced by fatigue. Films of the abdomen disclosed a group of four calcified nodes on the right side of the 3rd and 4th lumbar bodies which were not present on the films taken six years previously. A small intestinal study, June 9, 1932, disclosed hypermotility of the jejunum and delay in the ileum. Barium reached the lower ileum in one and a half hours and did not begin to enter the cecum until five and a half hours; at nine hours considerable opaque material remained in the ileum. The calcified nodes were not tender and were not as freely movable as the ileum. The patient has been fairly comfortable under medical observation except when he overworks.

Case vi. (Unit No. 333075). An obese nurse, aged twenty-two, for one and a half years had occasional transient abdominal pains associated with nausea and not related to food. Finally, a severe attack accompanied by vomiting and slight diarrhea led to appendectomy, April 26, 1933. The appendix showed hemorrhage into the mucosa and submucosa but no histologic evidence of inflammation was present. The pathologist's diagnosis was "periappendicitis (?)." Convalescence was uneventful. Five months after operation she complained of almost constant abdominal pain with nausea. A barium meal, Sept. 18, 1933, disclosed irritability and hypermotility of the large intestine. The lower ileum showed very active peristalsis with scattered, separated rounded or oval masses of barium. There was marked generalized right lower quadrant tenderness. A chain of small calcified lymph nodes lay along the right side of the 3rd lumbar vertebra. A small intestinal study was done Sept. 21, 1933, films being taken every fifteen minutes. The barium reached approximately the middle ileum in one hour, stopped there for an hour and then began to pass on again. Roentgenoscopic examination at two and a half hours disclosed abnormal peristalsis and a tendency to spasm after the segmental movements in the loops of ileum adjacent to the calcified nodes. Extreme tenderness was present on pressure over these nodes. The loops of proximal and middle ileum were about half the size of the jejunum; the terminal ileum was normal in size. The pain continued. On Jan. 18, 1934, a severe attack occurred, followed by gradual improvement with two months' rest in bed. After another severe attack, July 12, 1934, the patient was operated upon. Numerous enlarged lymph nodes were scattered throughout the mesentery, the largest mass lying near the duodenojejunal angle. Some of them were partially or completely calcified. Scarred, contracted areas were scattered throughout the mesentery, particularly in the vicinity of the calcified nodes. Ten nodes were removed. The pathologist found no evidence of tuberculosis. His diagnosis was "chronic mesenteric lymphadenitis, calcification of the mesenteric lymph nodes." After the operation the patient was symptom-free for almost a year when she had a sudden attack of violent abdominal pain with vomiting. Roentgen examination disclosed marked, persistent pylorospasm without disease of the stomach and duodenum, and marked delay in the small intestine. The barium began to leave the stomach

in two hours and had not begun to enter the cecum at nine hours. After a week of rest in the hospital the symptoms again improved.

Case vii (Unit No. 339677). A boy, aged thirteen, was admitted to the hospital because of suspected appendicitis. From the age of five years on, he had attacks of gas and colic, and some digestive handicap which kept him from eating food as other boys did. In February, 1932, he was sent home from school because of abdominal pain and rigidity but the signs quickly disappeared. On May 2, 1932, a similar attack occurred. A tender mass was felt in the region of McBurney's point. A film of the abdomen showed a group of calcified lymph nodes lying on the right of the 5th lumbar vertebra. A small intestinal study, May 4, 1932, showed the barium in the lower ileum in one hour. On several films, loops of proximal or middle ileum overlying the calcified nodes were very narrow, about one-third or one-fourth the normal width, with ragged irregular margins. On roentgenoscopic examination they showed continuously active peristaltic movements. Marked tenderness was present over the calcified nodes. The terminal ileum showed exaggerated mucosal folds; it, the cecum and the ascending colon appeared irritable. At nine hours the ileum was empty but the stomach contained a barium residue. The irritability of the terminal ileum led me to suspect ileocecal tuberculosis. The pain continued and the patient was operated upon May 20, 1932. Free fluid was present in the peritoneal cavity. The cecal wall and distal ileum were possibly slightly thickened but nothing was seen to suggest tuberculosis. Calcified nodes were felt in the ileocecal angle and enlarged, non-calcified nodes were seen in the mesentery of the ileum. The appendix seemed slightly thickened and the vessels over it were injected. It was removed. The pathologist found polymorphonuclear leukocytes in the lumen of the proximal third and in the submucosa. He said, "I believe this might be considered a very early case of acute appendicitis in spite of the fact that the mucosa is intact and the muscular wall free from infiltration." Postoperative convalescence was uneventful. In this instance the question might be raised as to whether the narrowing of the loops of ileum was due to the calcified nodes or to a reflex disturbance from the early appendicitis. Unfortunately no follow-up history is available.

Fig. 5. Case vii. A group of calcified nodes lies to the right of the 5th lumbar vertebra. The loops of ileum overlying them are narrow and irregular in width. Continuously active peristalsis and wide areas of spasm were observed with the roentgenoscope. A six hour gastric residue was found.

COMMENT

All of these patients suffered from abdominal pain. They all had calcified mesenteric lymph nodes which, it seems probable, were directly related to the symptoms in Cases i, iii, iv, v and vi, but not in Case ii. In Case vii they might have had something to do with the pain and digestive disturbance suffered through childhood but probably not with the acute symptoms for which operation was performed; yet it must be noted that the acute appendicitis was in a very early stage. In Cases i, iv and vi, excision of calcified nodes interrupted a succession of attacks lasting as long as two or three years.

Various manifestations of disturbed small intestinal physiology were observed. Spasm in the loop or loops of small intestine adjacent to the nodes was noted roentgenologically in Cases i, iii, vi and vii,

and at operation in Case IV. Delay in the passage of barium at the site of the calcified nodes was found in Cases II, III, V and VI. A nine hour ileal residue was present in Cases I and V, and a twenty-four hour ileal residue in Cases II and III. Delay in the ileum was frequently associated with hypermotility of the proximal part of the small intestine. Active reversed peristalsis in the ileum—not a "pendulum" movement—was seen in Case III. Delay in the emptying of the stomach, apparently of reflex origin, was found in Cases III, IV, VI and VII.

The fact that two conditions occur together does not necessarily mean that one causes the other. However, these disturbances in small intestinal physiology seemed to take place in loops of intestine directly adjacent to calcified nodes. The puckering and contraction of the mesentery about them and the distortion of the blood vessels make it seem very likely that the nerve fibers are involved in the process. A mechanism for a disturbance in intestinal physiology would seem to be present. One manifestation of abnormal intestinal physiology observed in these cases is spasm, and spasm of the intestine offers at least one possible explanation for pain. Occasionally a patient says that pressure on the calcified node reproduces the pain for which relief is sought.

It may be pertinent in passing to discuss briefly the question of etiology of calcified mesenteric nodes. No other cause than tuberculosis has as yet been proved, to the best of my knowledge. However, it is of interest that (1) calcified nodes in which there is no reliable evidences of tuberculosis, even by guinea pig inoculation, are often associated with (2) enlarged, abnormal, non-calcified nodes in which no histologic evidence of tuberculosis is present. Guinea pig inoculation with material from such a node removed at the second operation in Case IV gave a negative result for tuberculosis. Furthermore, in this case at the second operation the small, tubercle-like, yet non-tuberculous elevations scattered over the visceral peritoneum were very like the small elevations found in association with nonspecific ileitis (Homans and Hass). In another case, not included in this report, a calcified node as well as numerous abnormal non-calcified nodes were associated with proved early non-tuberculous ileitis. Strömbeck believes that calcified mesenteric nodes are all of tuberculous origin and that they reduce the resistance of the regional lymphatic structures to non-tuberculous infection. While it is impossible to prove that a calcified node did not originally come from an acid-fast infection, the possibility of a non-tuberculous origin in some cases cannot as yet be ruled out.

SUMMARY

1. Seven cases are reported in which evidence of abnormal small intestinal physiology was associated directly with calcified mesenteric lymph nodes.

2. This abnormal small intestinal physiology was demonstrated by roentgen methods in six cases and at operation in one case.

3. It consisted of (1) localized spasm, i.e., narrowing of a small segment adjacent to the calcified node, either temporary following a peristaltic wave or persistent; (2) persistent generalized spasm of a group of small intestinal loops in the region of the diseased nodes; (3) delay in the passage of barium at the site of the calcified node; (4) delay in the emptying of the ileum for periods of over nine hours.

4. The possibility that this disturbed physiology in the small intestine may be one explanation for the symptoms often associated with calcified mesenteric lymph nodes is suggested.

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DISCUSSION

Dr. Lester Levyn, Buffalo, N. Y. Mesenteric lymphatitis has been recognized for many years as a definite clinical entity. Considering the relative frequency with which this condition is encountered, especially after calcification of the nodes has occurred, it is surprising that its importance has not been stressed to a greater extent by roentgenologists, since the recognition can only be made on the roentgenogram.

In 1928, Dr. Golden presented a very excellent paper before this Society on the "Clinical significance of calcified abdominal lymph nodes." Since that time it has been my practice not merely to mention their presence in passing but to emphasize to physicians the rôle of these glands as a probable factor in the production of abdominal symptoms of otherwise undetermined origin. In adults, the symptoms frequently are those of duodenal ulcer, gallbladder disease or renal calculus.

To my knowledge, Dr. Golden is the first worker to describe the changes that occur in small intestinal physiology due to calcified mesenteric nodes. The only change I have observed is reverse peristalsis in the duodenum which I did not attribute to the presence of the calcified nodes. After seeing the work of Drs. Ravdin, Johnston and Pendergrass in the Scientific Exhibit, I am convinced that it is very difficult in most instances to differentiate between normal and abnormal small intestinal patterns. These workers showed marked differences in physiology and patterns when various food substances were administered with the barium. The accuracy of our interpretation will depend largely upon the adoption of a standardized barium mixture.

I wish to reiterate the clinical importance of calcified mesenteric lymph nodes. Only last week I visited a moderately large tuberculosis sanatorium. The physician-in-chief was familiar with the so-called acute lymphadenitis. However, he was quite unaware that calcification of the mesenteric lymph nodes is apt to produce symptoms. Routine gastrointestinal studies are conducted on all patients in his institution. No preliminary scout films are made. His attention had never been directed to the shadows of calcified nodes. At the time, there were three adult patients at the sanatorium who suffered from occasional attacks of pain in the right lower quadrant, accompanied by vomiting and extreme weakness; no elevation of temperature during the attacks and no leukocytosis. In one, appendectomy had been performed during childhood. The doctor was very much interested and said he would request roentgenograms of the abdomen in these cases and advise me of the results on my return to Buffalo.

Dr. Golden is to be congratulated on his observations of the disturbance in small intestinal physiology as presented to us.

Dr. Howard E. Ruggles, San Francisco. In the past year we have seen three young girls under fifteen who had symptoms suggestive of chronic appendicitis, rather a typical lower right quadrant pain sometimes associated with vomiting. All three of them came to operation, presumably for appendicitis and all of them had acutely inflamed mesenteric glands which had not yet calcified so that there is no question that the acute stages give even more definite reflex symptoms than the calcified ones. Two of them were fluoroscoped before operation and the only positive findings were ileal stasis and fairly localized tenderness.

EMPHYSEMATOUS BLEBS AND BULLAE*

By EUGENE FREEDMAN, M.D.
CLEVELAND, OHIO

LIKE congenital cystic conditions of the lung, the emphysematous blebs and bullae have been given almost no consideration in medical literature. The number of roentgenologically diagnosed and subsequently proved cases is still small. The shadows that these emphysematous blebs and bullae cast on the roentgenogram belong to the so-called "annular shadows."

Fishberg[8] was one of the first authors to raise the question as to whether all the annular shadows, that are seen in certain lung roentgenograms—mainly in the apices—and that heretofore have been diagnosed as cavities, are cavities or are due to some pathologic conditions like localized pneumothorax. He felt that many of them were due to pneumothorax, but was not successful in proving his theory. Of a total of 8 cases, in 7 instances he called the annular shadows localized pneumothorax, but in the latter cases two post-mortem examinations were carried out and in both the shadows were proved to be cavities and not pneumothorax. Fishberg's paper, however, aroused the interest of American roentgenologists, and during the following years numerous publications appeared on the annular shadows and their significance. Sampson, Heise and Brown[19] in 1918 stated that many of the so-called "cavities" seen on the roentgenograms are not intrapulmonary lesions, but intrapleural, and are situated between the lobes or between the lungs and chest wall, representing interlobar hydro-, or pneumothorax, or localized pneumothorax. The authors felt that these structures changed very rapidly in size on the roentgenograms, while a cavity would not do this. Evans[5] in 1919 also admonished roentgenologists not to diagnose all ring shadows as cavities and demonstrated some shadows which he believed were due to pleural structures rather than to cavities.

Amberson[1] in 1924 stated that annular pleural shadows were realities which must be distinguished from intrapulmonary cavitation. The lesion casting such shadows appears most often caused by localized pleurisy, which undergoes rapid changes in size. These publications swung the pendulum in the other direction, and while previously every ring shadow on a chest roentgenogram was diagnosed as a cavity, during the following years many of the typical ring shadows were considered to be due to hydro- or pneumothorax.

Despite the numerous roentgenologically demonstrated cases of localized apical pneumothorax, there was no further report that any of these lesions were proved at autopsy, and gradually the diagnosis of localized apical pneumothorax appeared more and more infrequently in the reports of competent roentgenologists.

Laurell[14] was the first to prove experimentally that emphysematous blebs and bullae cast ring-shaped shadows on the roentgenogram. He concluded from his experiments that very likely some of the ring shadows which in the early periods of roentgenology were indiscriminately called cavities and some of them which later were called localized pneumothorax or pleural rings on account of their changeable size were really due to emphysematous bullae or blebs.

Although both blebs and bullae represent localized air pockets within the lungs, they differ from each other as far as location is concerned. The blebs are situated immediately underneath the pleura while the bullae are in the lung tissue itself.

According to Miller[15] in a case of bleb there is a rupture of the subserous layer of

* From the Roentgenological Service of the University Hospitals and City Hospital, and the Western Reserve University School of Medicine, Cleveland, Ohio.

the connective tissue of the pleura which is composed of collagenous and a few elastic fibers and the escaping air from the ruptured alveolus separates the pleura proper from the underlying alveoli. The rupture of the alveolus occurs at a point where the elastic fibers of the alveolar wall have given way, possibly from having been stretched to the breaking point. The air, having gained admission into the alveolar layer and having caused it to separate from the walls of the underlying alveoli, extends along the pleura in the same manner as a dissecting aneurysm extends along the wall of an artery. Miller found a well-marked emphysema in every case in which emphysematous blebs occurred.

The bullae are also caused by ruptured alveoli, but in these cases the atrophic and dilated alveoli rupture one into another, coalesce and allow the formation of smaller or larger intrapulmonary air pockets.

In the case of the bleb the pleura is separated by the air from the underlying alveolar walls. In the case of bullae the pleura retains its connections with the lungs, although the alveoli beneath it give rise to a bulla through rupture and fusion.

According to Fischer-Wasels,[7] isolated blebs and bullae may occur in connection with local indurative and productive changes in any part of the lungs without a generalized emphysema. He calls these "scar tissue vesicles" and explains their formation by localized inflation and atrophy of the lung tissue caused by valve-like structures. These valves develop as a result of a small, localized inflammatory process with subsequent scar formation, producing a constriction of the bronchioles with atrophy and deformity of the corresponding lung tissue. In the apices they commonly occur in connection with shrinking tuberculous processes. Hayashi,[10] on microscopic examination, found these valve-like structures at the bases of the vesicles. Their microscopic appearance was that of deformed, atrophied lung particles. These valves allow the air to pass freely into the vesicle, but prevent it from passing out again. The effect is that the vesicles gradually increase in size and finally rupture into either a neighboring alveolus or the subpleural areolar tissue. These air vesicles develop not only in consequence of localized scar tissue but also in the presence of foreign bodies, mucous or pseudomembranous plugs of exudate in the bronchi.

Bullae and blebs may occur at any age. They have been found in children, whose lungs rupture more easily than those of adults, especially in assocation with conditions where an extensive mechanical misuse of the lung has occurred (pertussis, pneumonia, asthma, etc.).

Gielczyński[9] demonstrated numerous pearl-like air bubbles on the pleural surface of the chest of an infant who died of bronchopneumonia. Similar blebs were found near the right hilus and in the anterior mediastinum. The patient also had a pneumothorax on the right and a subcutaneous emphysema in the anterior portion of the chest and the neck. Gielczyński explained the findings as a rupture of a distended emphysematous alveolus, from which the air extended into the pleural cavity, mediastinum and eventually into the soft tissues of the neck and thorax.

Jäderholm[11] found in the roentgenogram of the chest of a boy, aged eighteen, an area of increased radiability throughout the left base. In this area only a few gracile lung markings could be seen. Later lipiodol was injected into this part of the lung and the bronchi were found to be normal. The author concluded that no other explanation than that of a bullous emphysema could be given for the changes. It was impossible to determine the mode of development, but the author suggested that it was most likely the end-result of one of the patient's previous attacks of pneumonia.

Laurell,[14] who experimentally produced blebs and bullae in excised calves' lungs by inflating air into the trachea, found that emphysematous bullae, as a rule, were less distinctly visualized on the roentgenogram than blebs, especially if they were

situated in a part of a lung that was already the site of a marked generalized emphysema. He also found that blebs and bullae did not always produce roentgenologically recognizable changes. At times the shadows cast by these structures are linear, vacuolated in type simulating bronchiectasis; others, of course, are circular. Some of the small blebs and bullae may cast patchy shadows suggesting the roentgenological appearance of areas of bronchopneumonic consolidation. The subpleural blebs usually form circular, ring-shaped shadows. Based on histological findings Laurell explained the ring shadows on the roentgenograms as being produced by a zone of atelectasis in the neighboring alveoli caused by the pressure of the air pocket.

According to recent investigations the emphysematous blebs and bullae play an important part in the production of spontaneous pneumothorax in the healthy individual. Orth[17] has given an accurate microscopic description of these vesicles, but no particular significance was attached to them. Hayashi[10] and Fischer[6] and Fischer-Wasels[7] demonstrated first that these vesicles may give rise to spontaneous pneumothorax. Cummer,[3] Dorendorf,[4] and Reiche[18] believed previously that spontaneous pneumothorax was produced by latent, nondemonstrable tuberculosis.

Kjaergaard,[13] in his excellent monograph on spontaneous pneumothorax, arrived at the conclusion that spontaneous pneumothorax in the apparently healthy lung was due to the rupture of a valve vesicle on the surface of the lung. His conclusions are based on 6 cases which came to autopsy. In each of these cases the pneumothorax was found to be due to the rupture of a solitary valve vesicle at the apex of the lung, with or without scar tissue, but without any demonstrable sign of an active tuberculosis.

He also made a careful study of 51 cases of spontaneous pneumothorax; 49 of these patients were followed by systematic roentgen examinations for at least three years and only one of them developed pulmonary tuberculosis subsequently.

Obstructive processes of the trachea or bronchi caused by either intrinsic or extrinsic lesions may lead to formation of blebs and bullae even in the absence of a generalized emphysema.

Apparently emphysematous bullae and blebs are not uncommon. According to Laurell[14] the reason that they are not seen more often at autopsy is that they are seldom the cause of death.

The roentgenological features of the blebs and bullae in 5 cases, 4 of which came to autopsy, are presented herewith. In 4 of them the roentgenological diagnosis of emphysematous blebs or bullae was made and in one case the bulla was thought to represent a tuberculous cavity.

CASE REPORTS

Case 1. A colored male, aged thirty-five, was admitted to City Hospital complaining of having had a slightly productive brassy cough for the preceding few months associated with shortness of breath. There was no hemoptysis. He felt as though someone was choking him and he had to hold his head forward to relieve this pressure. He had had chancre in 1916 and received some antiluetic treatment at that time.

Examination showed a retraction of the sternum and intercostal spaces during inspiration. Expiration was less labored. All accessory respiratory muscles were in use during respiration. Auscultation revealed a marked inspiratory stridor. Percussion revealed a marked aortic widening. The cervical veins were found engorged and a good tracheal tug could be elicited. The Wassermann reactions were four plus.

A combined roentgenoscopic and roentgenographic examination showed a circular shadow in the upper mediastinum which was interpreted as either an aortic or an innominate aneurysm.

The lung fields showed a peculiar variation from normal. The entire left apex and subapical region were occupied by a large area of increased brilliancy (Fig. 1), in the midst of which only a few lung markings could be seen. The lower border of this area was represented by a downward convex, hairline-like area of increased density. A few similar curved linear shadows could be seen throughout the middle third of the left lung field and throughout the right upper lobe. The right upper lobe also

contained a few smaller areas of increased radiability. In addition, the rest of the lung fields contained numerous, straight linear shadows of increased density intersecting each other, producing a bizarre pattern and extending from the hila toward the lateral chest wall and both bases.

The appearance of the upper lobes suggested air-containing hollow spaces in the lungs. The walls of these air-containing areas were of hairline thinness, finely curved and occupied the upper lobes, even in places where they did not seem to surround increased air-containing areas. The type of the other linear shadows in the dependent portions of the lungs was entirely different, the latter being thicker and straight, and it was thought that there were two distinct lesions in the lungs. The appearance suggested large emphysematous blebs in both upper lobes combined with a non-tuberculous extensive fibrotic process throughout the dependent portions of the lungs.

At the autopsy, by Dr. Herbert Reichle, an aneurysm of the transverse arch of the aorta at the exit of the innominate artery was found which pressed on the trachea, and produced two shallow ulcers on its mucous membrane just above the bifurcation.

The anterior border of the left lung was found markedly lobulated. These lobules appeared to be overinflated and did not collapse even when the ligature was removed from the trachea. Similar overinflated areas were found on the anterior surface of the right lung also. Upon opening the sacs, loose strands of fibrous tissue were found adherent to all walls of the sac. Incision into the other bullae also showed overinflated areas of lung tissue rather than cavities. Cut section of both lungs revealed a remarkable increase in connective tissue, the strands of which were arranged in a bizarre fashion. Anthracotic pigment was found everywhere. The pathological diagnosis, in addition to the aneurysm, was giant emphysematous bullae, generalized emphysema and anthracotic fibrosis of the lungs.

The microscopic examination showed an extensive and severe alveolar emphysema, rupture of the alveolar walls and formation of bullae.

Case II. C. M., a white male, aged sixty-four, was admitted to the University Hospitals on November 7, 1934, complaining of paralysis of the right arm and leg of four weeks' duration, with gradually increasing dyspnea, slight cough and no expectoration. On clinical examination signs of aortic dilatation were found. The blood Wassermann test was four plus, but the spinal fluid examination was negative.

The chest was emphysematous, barrel shaped with resonant percussion note everywhere. There were a few scattered inconstant crepitant râles at both bases.

Roentgen studies on November 11, 1934, revealed a marked dilatation of the entire aorta with numerous calcified plaques along the posterior and lateral wall of the descending

Fig. 1. Case I. Roentgenogram showing a large area of increased brilliancy in the left apex and subapical region. There are numerous smaller, similar areas throughout the right upper lobe. All of them are demarcated by fine curved lines of increased density and represent emphysematous bullae. The large mediastinal shadow is due to an aneurysm of the innominate artery. The intersecting linear shadows throughout the lower lung fields are due to an anthracosis.

aorta. There was a fusiform aneurysm in the midportion of the descending aorta measuring about 10 cm. in length and 4.5 cm. in width. In the apex of the right lower lobe, near the hilus, there was an irregularly circular structure measuring about 4 cm. in diameter, which considering the entire clinical picture and the fact that it did not cause any subjective or objective symptoms, despite its size, was thought to be possibly due to a syphilitic gumma.

The lung fields showed increased radiability,

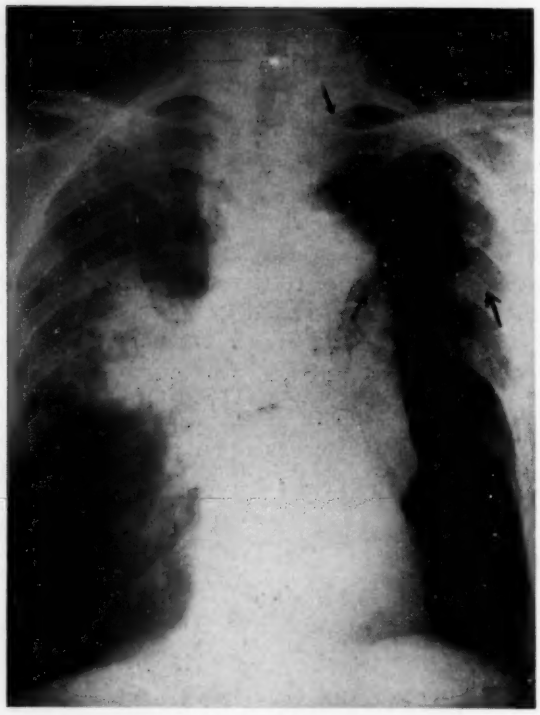

Fig. 2. Case II. Roentgenogram showing numerous emphysematous blebs or bullae in left upper lobe (arrows) represented by an area of increased brilliancy and by fine, curved, linear shadows. There is marked generalized emphysema. There is an aneurysm of the descending aorta. There is a possible gumma in the apex of the right lower lobe.

increased markings and wide intercostal spaces, due to an emphysema. In addition the left apex and subapical region showed an unusually marked translucency with an almost complete absence of the lung markings. Only a few gracile curved and linear shadows were seen to traverse this area (Fig. 2). On account of the marked emphysema elsewhere in the lungs, the absence of any clinical symptoms and the marked similarity of the roentgen changes between this case and Case I, multiple emphysematous blebs were suggested as the cause of the changes. There was another similarity between Cases I and II, i.e., the presence of an aortic aneurysm. The other similarity consisted in the apical situation of the blebs. This situation can be explained by the fact that the respiratory excursions in these regions are less extensive than in the lower thoracic regions on account of the more fixed position of the upper ribs. Hence, in a case of pressure by an aneurysm on one of the major bronchi, the stagnation of the air will be more marked in upper parts of the lungs, and emphysematous blebs and bullae will be more likely to develop there.

Case III. A white male, aged fifty-one, was admitted to the University Hospitals on August 11, 1934. He had not felt well for the preceding six months; the main symtpoms were weakness, cough and purulent expectoration. He had begun to expectorate blood-streaked sputum four months previously and had frank hemoptysis just before admission. The total loss in weight during the preceding few months was 25 pounds.

The physical examination revealed an emaciated man sitting in an orthopneic position, breathing as if he had obstructed air passages. The dyspnea was exceedingly marked but there was no evidence of cyanosis. The right chest was markedly restricted in its movements. Over the right middle and lower lobes there was a dullness but not flatness. The breath sounds over this area were suppressed, and the tactile fremitus was impaired. The entire clinical picture was suggestive of a malignant tumor in the lung.

A roentgenogram taken on August 13, 1934, showed a dense, mottled consolidation throughout almost the entire distal half of the right lung. The right diaphragm was displaced upward and the heart and trachea to the right indicative of some collapse of the involved lung. The upper mediastinum was enlarged to the right and lobulated in appearance.

A little to the right of the right hilus there was a fine, medially convex, linear shadow of increased density, the anatomical situation of which did not correspond with any of the interlobar septa. Lateral to this line the lung between the fifth to eighth posterior ribs showed a roughly circular area of increased brilliancy. This area measured about 6 cm. in diameter and except for its medial border it was not well demarcated (Fig. 3). The left lung was clear.

A roentgen diagnosis of primary malignancy of the right main bronchus with metastatic nodes to the mediastinum and partial collapse of the right lung was made. The area of diminished density with the fine linear curved medial border was considered to be suggestive of an emphysematous bleb.

At autopsy, by Dr. Alan R. Moritz, the right major descending bronchus was found to be completely encased in a grayish-white firm tumor, measuring 7×4 cm. in diameter.

Large metastatic tumor masses were found in the upper mediastinum. On the posteromedial surface, corresponding to the site of the area of increased brilliancy on the roentgenogram, an ovoid mass measuring 5 cm. in diameter was found. This area contained air and upon section revealed a wall made up of lung substance and pleura, due to an emphysematous bulla.

Microscopic section through the wall of the bulla revealed its outer surface to be covered with flattened mesothelium and the wall to be composed of a small amount of relatively acellular fibrous connective tissue, containing deposits of anthracotic pigment. The inner surface of the wall of the bulla consisted of compressed alveolar walls. A few ruptured septa projected into the lumen of the bulla. The surrounding lung showed emphysema.

Case IV.* D.S., white male, aged seven weeks, was admitted to the Babies and Children's Hospital of Cleveland on September 18, 1934, on account of difficulty in breathing since birth and failure to take food properly. About eight days before admission patient had convulsions lasting for five minutes.

* This case is published through the courtesy of Dr. H. J. Gerstenberger, Professor of Pediatrics, Western Reserve University, Cleveland, Ohio.

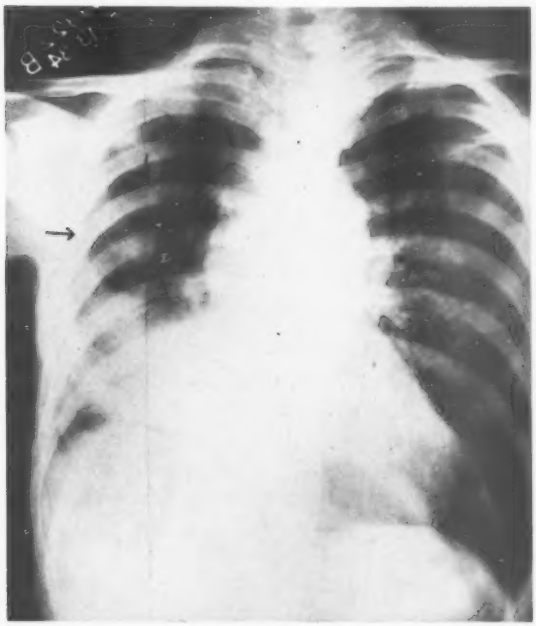

Fig. 3. Case III. Roentgenogram showing an emphysematous bulla in the middle third of the right lung (arrows). The lower border of the bulla is represented by a fine curved line. The mottling in the right base is due to a primary lung tumor and the enlarged mediastinum, to metastatic nodes.

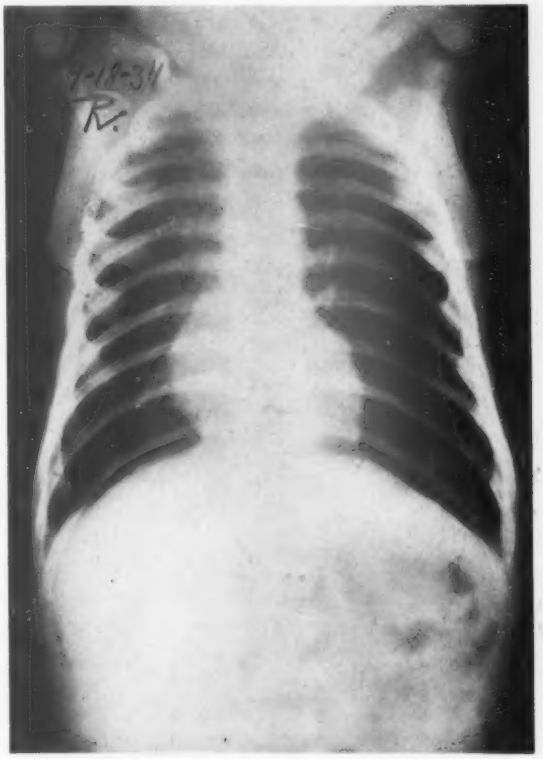

Fig. 4. Case IV. Roentgenogram taken during deep inspiration showing a marked emphysema throughout both lungs with a slight right displacement.

The respiration was forceful and almost purely costal in type. All the accessory muscles seemed to be employed. On inspiration there was a marked retraction of the suprasternal region. The expiratory phase was somewhat prolonged. The percussion note was resonant throughout and the breath sounds were normal.

The child's respiratory difficulty was so great that numerous possibilities were suggested, among which were paralysis of the diaphragm, anomaly of the diaphragm, diaphragmatic hernia, or a possible cerebral injury.

A roentgen study at the X-Ray Service of the Babies and Children's Hospital on September 18 revealed a marked depression of both leaves of the diaphragm. Their excursions were short and jerky. Both lung fields were very translucent, containing increased amounts of air and the intercostal spaces were wide, indicating an emphysema. No area of infiltration could be seen (Fig. 4).

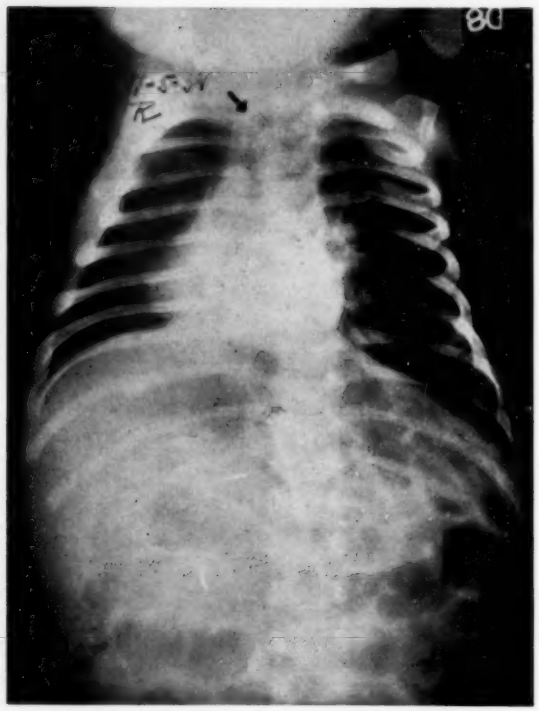

Fig. 5. Case iv. Roentgenogram taken in the expiratory phase forty-seven days later shows a semicircular linear shadow of increased density in the medial portion of the right apex. At autopsy an emphysematous bleb was found in the corresponding area. The right displacement of the heart is more marked than before.

At a subsequent examination on November 5, 1934, the diaphragms were higher in position than previously. The heart and trachea were displaced to the right. The lungs still showed increased translucency. This examination also revealed an outward convex linear shadow of increased density in the medial portion of the right apex, which measured about 4 cm. in length (Fig. 5). This shadow was thought to be due to an emphysematous bleb. No satisfactory explanation could be given for the marked emphysema at any of the clinical and roentgenological examinations.

At the autopsy, performed by Dr. E. B. Helwig, on November 5, 1934, trabecular mucosal thickening of the membranous urethra (urethral valves) was found with a marked secondary dilatation of the prostatic urethra. Both lungs were quite voluminous, the pleura was thin, smooth and glistening, revealing a pale, pinkish-gray color in the anterior portions. Upon sectioning, the dependent portions showed a purplish-red color, were somewhat increased in consistency and the seat of a moderate atelectasis. This was most prominent in both lower lobes. The anterior portions of both lungs, but predominantly the upper lobes, were the seat of marked emphysematous change. In the medial part of the anterior surface of the right upper lobe there were a few emphysematous blebs, involving an area measuring about 3.5 cm. in diameter (Fig. 5). The bronchial tree and its radicles were free of pathological changes.

Microscopical sections of the lower lobes revealed the alveoli in many instances to be collapsed and the interalveolar septa to be thick. In some instances the alveoli were edematous and contained red blood cells and a few histiocytic cells. No acute inflammatory changes were observed. In sections of other parts of the lung the alveoli were spacious, air-containing and the interalveolar septa were occasionally ruptured. The alveoli for the most part were empty and the bronchi and bronchioles showed some desquamation of the lining epithelium. Unfortunately no sections were taken from the site of the emphysematous bullae.

Consequently the picture was that of a combination of atelectatic patches throughout the lower lobes, with a marked bleb formation in the right apex. The atelectasis was very likely a contributing factor in the subsequent development of the emphysema. It could not be definitely determined whether or not the atelectasis was congenital or acquired, although the history of difficulty in breathing since birth appeared to favor the former supposition.

Case v. A white male, aged thirty-five, was admitted to Cleveland City Hospital with a history of cough and expectoration of mucopurulent sputum for the preceding months.

Roentgenograms taken of the patient's chest on October 11, 1933, disclosed an advanced fibro-ulcerative tuberculous process throughout the proximal two-thirds of the right lung and an extensive fibrotic process throughout the upper half of the left lung. Both hila were retracted upward and the trachea was displaced to the right.

On a subsequent examination, three months later, there was an additional pleural effusion encapsulated throughout the lateral portion of the left base. This examination also revealed a ring-shaped area of increased density in the lateral portion of the left subapical region

which measured about 5 cm. in diameter. The thickness of the wall of this shadow measured about 2 or 3 mm. The ring-shaped shadow surrounded a similar-shaped circular shadow of diminished density (Fig. 6). On the previous examination this was not present and the appearance indicated a cavity in the left apex that had developed during the preceding three months.

The patient died on January 30, 1934, and the post-mortem examination, by Dr. Herbert Reichle, revealed a chronic conglomerate tuberculosis of the right upper, and left upper and lower lobes. These were numerous cavities in the right upper lobe. However, the shadow in the left apex, which had been interpreted as a cavity, proved to represent an emphysematous bleb measuring 5 by 2.5 by 4 cm. in diameter (Fig. 7).

DISCUSSION

The foregoing cases show the types of shadows that some emphysematous blebs and bullae may cast on the roentgenogram.

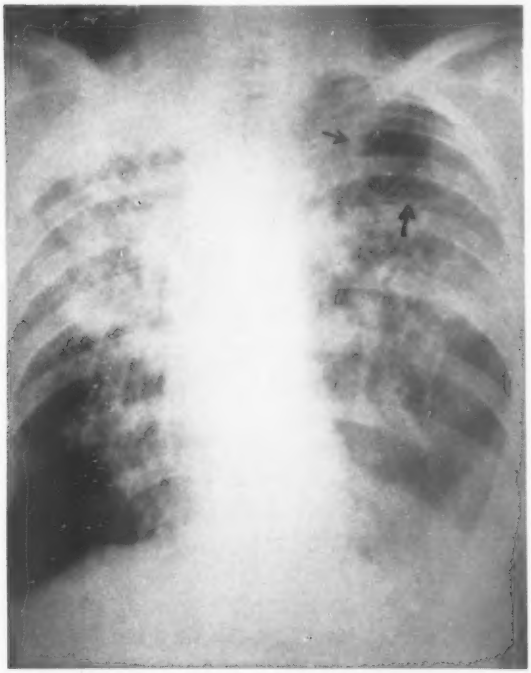

Fig. 6. Case v. Roentgenogram showing a dense mottling throughout the proximal two-thirds of both lung fields, due to an extensive tuberculous process. There are numerous small cavities in the right upper lobe. The cavity-like structure in the left apex (arrows) is due to an emphysematous bulla.

Fig. 7. Case v. Photograph of vertical section of left lung showing a conglomerate tuberculous process in the entire upper lobe and emphysematous bulla in the lateral portion of the apex (arrows).

In the first case the number of curved shadows around the shadows of diminished density aroused the suspicion that they represented something other than cavities. The thinness of the marginal shadows was also unusual for cavity walls, and there was no evidence of sufficient amount of consolidation in the upper lobes to justify the diagnosis of cavity. Pneumothorax was also considered but there was no clinical history of a previous artificial pneumothorax. A spontaneous bilateral pneumothorax was excluded because of the great number of the shadows, and the patient did not give a history of a sudden onset which is almost always present in cases of spontaneous pneumothorax.

The presence of a large aneurysm accom-

panied by excessive shortness of breath was also of aid in establishing the diagnosis. There was no question that the production of the blebs was caused by the combination of three factors, as proved at the autopsy, the fibrosis produced by the pneumoconiosis, the extensive emphysema secondary to the pneumoconiosis and the pressure on the trachea by the innominate aneurysm, causing a ball-valve obstruction in an already severely damaged lung which had all the conditions for the spontaneous formation of an emphysematous bleb even without the additional obstruction of the trachea.

The second case showed many similar features both clinically and roentgenologically.

In the third case the bleb was single and was situated near the right hilus. Its roentgenological recognition was aided by the finding of a circular area of brilliancy in the upper part of the lung, which was already the site of an obstructive emphysema. The medial border of this area was formed by a semicircular hairline shadow of increased density. Its lateral border was not sharply demarcated. The lower half of this lung showed evidence of tumor formation and the upper mediastinum contained numerous metastatic nodes. The autopsy revealed an emphysematous bulla at the corresponding site.

The fourth case showed only the outer wall of the emphysematous bleb represented by a semicircular curved shadow. Its diagnosis was facilitated by the serial examination and by the presence of the extensive generalized emphysema. The development of the bleb was very likely secondary to a congenital atelectasis.

The fifth case illustrates one of the pitfalls in the diagnosis of cavity. Here there were all the essential roentgenological requisites for a diagnosis of cavity. The patient had a considerable amount of consolidation in both upper lobes, and many cavities in the right upper lobe, and between two examinations, with an interval of three months, there developed what appeared both roentgenographically and roentgenoscopically to be a cavity on the left side. The wall of the bleb was also rather thick, measuring about 2 mm., considerably thicker than the walls in the preceding cases.

Miller[16] published the report of a similar case recently where the deceptive appearance of a large emphysematous bulla led to an erroneous diagnosis of tuberculous cavity.

Arnell[2] also stated that formations other than cavities due to dissolution of pulmonary tissue or the pathologically extended bronchus can be the cause of annular shadows. But many cases of annular shadows will be diagnosed as cavernous tuberculosis which are cases of innocuous subpleural or interstitial emphysematous blebs. Many of the so-called mute cavities in the lungs are perhaps such comparatively harmless formations.

The diagnosis of emphysematous blebs or bullae can be made with relative ease in some cases. In others their correct interpretation is difficult or impossible, mainly if they develop in a part of a lung which is already the site of tuberculous infiltration.

A localized pneumothorax can be differentiated from a bulla or bleb by the fact that in the latter, despite the area of increased brilliancy and lack of normal lung markings, no shadows can be seen which would indicate the contour of a collapsed lung.

In differentiating congenital cysts of the lung from emphysematous blebs or bullae one has to pay special attention to the walls of these structures, which are rather coarse and often finely frayed out in cysts, while in blebs or bullae they are very fine, hairline-like in thinness and sharp. Evidence of a generalized emphysema of an aortic aneurysm, shadows suggesting a lung or a mediastinal tumor, atelectatic patches, areas of pneumonic consolidation should all be brought into relationship with the finely curved ring and oval shadows, since these are some of the conditions which by interfering with the normal res-

piration lead most commonly to the formation of emphysematous blebs or bullae. A thorough knowledge of the clinical history, i.e., the knowledge of the presence or absence of asthmatic attacks or of a previous acute respiratory disease associated with strenuous cough may be helpful at times.

CONCLUSIONS

1. Emphysematous blebs and bullae are often recognizable on the roentgenogram as localized areas of increased brilliancy in the lung fields, surrounded most commonly by thin hairline-like curved and annular shadows which are due to a zone of atelectasis in the neighboring alveoli caused by the pressure of the air pockets.

2. The lungs need not show the roentgenological evidence of generalized emphysema since blebs and bullae are occasionally found in the absence of a generalized emphysema. In the latter cases, the air pockets are usually secondary to localized scar tissue.

3. Attacks of asthma or of strenuous cough, aortic aneurysms, mediastinal or lung tumors, patches of atelectasis or of pneumonic consolidation may lead to the formation of blebs and bullae by interfering with the normal respiratory mechanism.

4. Occasionally an emphysematous bleb or bulla may closely simulate a tuberculous cavity.

5. It is surmised by various authors that some tuberculous cavities may have been originally emphysematous blebs, which had been secondarily infected.

6. Emphysematous blebs and bullae play an important rôle in the production of spontaneous pneumothorax.

7. There is a possibility that the so-called annular shadows which were previously considered to be due to encapsulated, localized pneumothorax, mainly on account of the rapid decrease in their size, were due to emphysematous blebs and bullae.

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THE ROENTGEN TREATMENT OF MALIGNANCY USING FILTRATION EQUIVALENT TO 5 MM. COPPER*

By E. A. MERRITT, M.D., *and* R. RHETT RATHBONE, M.D.
Warwick Clinic and Garfield Memorial Hospital
WASHINGTON, D. C.

THE desirability of increasing filtration above 0.5 mm. copper at voltages at or near 200 kv. (peak) is still controversial, notwithstanding the very substantial contribution by Coutard[1] favoring heavier filters. Those who deny the value of increased filtration do so on the premise that filtration above 0.5 mm. copper represents wasted energy. Most observers who have had an opportunity to compare skin reactions and results obtained with 0.5 mm. and 2.0 mm. copper filtration are convinced of the latter's superiority. The purpose of this communication is to set forth our experience with a 200 kv. (peak) apparatus and to support the thesis that the results we have obtained justify further investigation by actual clinical application of such voltages with filters as heavy as 5 mm. copper or its equivalent.

Following the work of Thoraeus[9] we have made and, for the past fifteen months, have been using at the Warwick Clinic a filter composed of 1.25 mm. tin, 0.25 mm. copper and 1.0 mm. aluminum. This filter has been used at 220 kv. (peak) (180 kv. effective), 20 ma., 50 cm. distance, with an intensity of 10 roentgens per minute (measured in air). This filter has a maximum wave length as defined by Thoraeus of 0.21 Å which is the same maximum wave length as 5 mm. copper. We have made copper absorption curves and this filter has a half-layer value of 2.9 mm. copper at 220 kv. (peak) which is the same as 5 mm. copper at this voltage. The effective wave length is 0.086 Å. This tin filter is very transparent to hard roentgen rays generated at 220 kv. (peak) and gives an intensity 35 per cent greater than 5 mm. copper. With this filter we have found the intensity of 10 r per minute at 50 cm. distance to be practical and economical in the treatment of selected deep-seated malignancies. We have also been treating a number of skin and relatively superficial malignancies (lip, buccal mucosa, metastatic cervical glands) at 25 cm. distance with an intensity of 40 r per minute with this filter. Are the therapeutic results sufficiently superior with this increased filtration to justify its use? We believe thay are.

In radium therapy, for a number of years, we have, in common with others, discarded the dictum that 2 mm. brass is sufficient filtration and have increased the filtration to 1 mm. and 2 mm. platinum. This has been done for several reasons. Much larger doses can be given safely because the permanent damage to underlying subcutaneous tissue is less and the results appear to be improved. This brings up the problem of a differential biological reaction to short wave lengths, a concept that physically seems improbable and is denied by many because experiments with *Drosophila* eggs and wheat seedlings have demonstrated that the reactions with such test objects are independent of wave length. These physical considerations and experiments are opposed to our clinical observations that there is a differential biological reaction resulting from heavier filtration and therefore dependent upon wave length. There is support for our clinical observations in the published investigations of Russ and Scott[7] who draw three definite conclusions from their experiments: (1) that the reactions caused in the skin and tumor depend not only on the amount of energy absorbed by the tissues but upon the particular wave lengths of

* From the Radiologic Clinic of Drs. Groover, Christie and Merritt.

the radiation; (2) the extent of this differential action appears to depend upon the nature of the tissue, and (3) because of the change in the right direction (more effective on tumor) of the differential factor it seems to be more satisfactory to use short wave length radiation for any subcutaneous growths.

From our experience with protracted fractional irradiation with hard radiation (0.21 Å maximum wave length, 5 mm. copper equivalent filter), we believe that there is a differential effect on skin or epidermoid structures as a group in contrast to connective tissue or the supporting body structures as the other group. When 0.5 mm. copper filtration is used there is a moderate difference in the lethal dose between skin and the underlying subcutaneous tissues. As the filter is decreased, with a corresponding softening of the beam, we believe the lethal doses for skin and for the underlying connective tissue approach each other but never meet. Conversely, as the filtration is increased to 5 mm. copper, there is a marked widening of the lethal doses for skin and for subcutaneous tissue. Thus we feel that increasing the filtration is the best method at our disposal for protecting the underlying subcutaneous tissues when giving a lethal skin dose. In our treatment of superficial malignancy we are impressed with the necessity of producing complete destruction of the skin, as we have yet to permanently destroy a squamous cell carcinoma with less than a blistering dose equivalent to a first degree burn. In the production of these reactions for large areas (15×5 cm. and over) heavy filtration is a necessity to insure healing. Heavy filtration is neither necessary nor advocated in giving blistering doses to very small areas, unless cartilage is eroded or involved. These conclusions are based upon our daily observations in the treatment of skin carcinoma where we can readily observe the immediate and late effect upon both the tumor and the tumor bed.

In treating opposing fields, particularly the head and neck, where there is from 25 to 50 per cent transmitted radiation from the opposite side, widening of the lethal threshold between skin and subcutaneous tissues is not readily observable because, as Quimby and McNattin[5] have shown, this transmitted radiation is very soft, even though high initial filtration is used. This soft transmitted radiation greatly reduces the total amount of radiation that can be safely given to the opposing skin surfaces as its destructive effect on skin and adjacent supporting structures is practically identical.

We believe that the function of filtration has been much neglected in radiation therapy. We have paid too much attention to voltage or the short wave lengths in the beam and have thought very little of the long wave lengths which are determined entirely by the filter. Theoretically, the best filter is the heaviest filter we can use economically, as skin effect is determined almost entirely by the long wave lengths in the beam of radiation, plus the back-scattering. The function of filter is to remove these long wave lengths and at the same time harden the beam which thereby decreases back-scattering. In our use of different filters we are impressed with the importance of employing as hard radiation as is economically possible.

For years one of us (Merritt) has been giving intense blistering doses of roentgen radiation, producing an epidermolysis, with filtration varying from unfiltered radiation to 1 mm. copper. This has been done both with single massive doses and with protracted fractional irradiation. The reactions all appear about the same at their height; it is in their healing and late effects that one observes the great difference in contrast to heavier filtration. If light filtration is used there is a profound modification of the underlying supporting skin structures as evidenced by slow healing, intense pain, and finally when healing does occur there is atrophy and marked telangiectasis. With this background of reactions we are impressed with the mild

modification and damage to the supporting skin structure when these same blistering or epidermolytic doses are given with filtrations of 2 mm. copper, and more particularly with the equivalent of 5 mm. copper. Such observations leave no doubt in our minds as to the presence of a differential effect with harder radiation.

The principal factors in the Coutard method of radiation therapy are: (1) intense epithelitis and epidermitis; (2) low intensity per minute; (3) daily treatment over several weeks' time, and (4) the use of heavy filtration of about 2 mm. copper. In our experience, at 220 kv. (peak), filtration equivalent to 5 mm. copper is preferable in radioresistant tumors and in deep-seated tumors. This filtration is available to every radiologist with a machine capable of running from 20 to 30 ma.

The problem of low intensity per minute is unsettled. In our experience with intensities ranging from 10 to 75 r per minute and with our goal in dosage set as an intense epidermitis and epithelitis, we have noticed no change with intensity in the relative lethal dose for skin and subcutaneous tissues. This is important economically because since we have observed no decrease in subcutaneous tissue tolerance with high intensities we can give our treatments in a few minutes rather than hours. In the treatment of extensive superficial malignancies involving cartilage, we use a 25 cm. distance and an intensity of 40 r per minute, which means a daily treatment time of six minutes to deliver the average dose of 240 r with the filter equivalent to 5 mm. copper.

The problem of the total treatment time in days is also unsettled. We, in common with others, feel that protraction of treatment time in days increases the relative subcutaneous tissue tolerance to irradiation. If the time is protracted too long, or approximately nine weeks, there is danger of tumor recovery. The daily and total dose must be so adjusted as to exceed the recovery rate or the so-called tolerance dose. We believe this tolerance dose to be about 150 r per day to a single area with this heavy filtration. We believe relatively sensitive malignancies can be easily destroyed with a high daily dose in about three weeks' time; if, however, the malignancy is relatively resistant the time should be protracted over four to six weeks with a lower daily dose and higher total dose.

When a lethal skin dose is given with the equivalent of 5 mm. copper filtration, the reaction is slow in coming on and complete destruction of the skin is not observed until about the thirty-seventh day after beginning treatment. The reaction appears violent as there is complete vesiculation of the entire epidermis. In contrast to this violent destruction of the skin, there is very little edema of the corium and, what is most important in treating patients, there is practically no pain. Healing occurs in about six to twelve weeks, epithelization occurring from numerous islands of epithelium and from the borders. Finally, unless the lethal threshold for subcutaneous tissues is exceeded, there is none of the hard, brawny induration that follows when a lethal skin dose is given with filtration of approximately 0.5 mm. copper. It is the observation of these reactions, during the course of treatment and afterward, that convinces us that harder radiation widens the lethal threshold between epithelium and supporting skin structures. As a corollary of this widened threshold comes the important application of this type of radiation to epidermoid carcinoma. The cell of origin of malignancy is of prime importance in determining its degree of radiosensitivity. If it is possible to destroy skin structures, it follows that it will be possible to destroy epidermoid carcinoma or any malignancy with the same degree of sensitivity as skin with less permanent damage to the surrounding structures. We[4] believe this to be true from observation of superficial malignancies treated with 2 mm. copper and, from more recent experience, using the equivalent of 5 mm. copper.

With these clinical and biological considerations as the indications for heavier

TABLE I

COMPARISON OF THE 10 CM. DEPTH DOSE FOR CONSTANT 10×10 CM. FIELD WITH VARIABLE VOLTAGES, DISTANCES AND FILTERS

Quimby	*Quimby*	*Taylor and Tucker*	*Mayneord and Roberts*	*Leucutia and Corrigan*
200 kv. (peak)	200 kv. (peak)	200 kv. (peak)	400 kv. constant	550 kv. constant
50 cm. distance	50 cm. distance	104 cm. distance	75 cm. distance	60 cm. distance
0.5 cm. copper	4.4 mm. copper	0.6 mm. copper	5.0 mm. copper	approx. 6.6 mm. copper
32.6%	37.6%	38.0%	43.0%	44.5%

filtration in general, let us examine the possibility of treating deep-seated lesions and compare the depth dose obtainable with that of much higher voltages. We realize that there are many unavoidable errors in depth dose measurements and, due to our present inability to measure hard and soft radiation accurately, they may in the future be revised. They are, however, our only physical guide at present as to what goes on in the deep structures.

We have made no measurements of depth dose at 10 cm. using a filter of 1.25 mm. tin, 0.25 mm. copper and 1.0 mm. aluminum. However, Quimby and Marinelli[6] have made measurements at 200 kv. (peak) and 4.4. mm. copper which are applicable, and Mayneord and Roberts[3] and Leucutia and Corrigan[2] have made measurements at much higher voltages. Taylor and Tucker[8] have also made measurements at 104 cm. distance which are interesting (see Table 1).

As shown in Table 1 the 10 cm. depth dose is 37.6 per cent for filtration slightly less than 5 mm. copper. This is also approximately the same depth dose obtained at 104 cm. distance with 0.6 mm. copper at 200 kv. (peak). The time relations about balance each other as our machine delivers 11 r per minute at 100 cm. distance with 0.5 mm. copper filter and 10 r per minute at 50 cm. distance with 5 mm. copper equivalent filter. The fact that the skin and the subcutaneous tissues will tolerate tremendous doses of roentgen rays with the heavy filtration convinces us of the superiority of increased filtration over increased skin target distance. We have safely given 5,000 r (measured in air) to a single 20 × 20 cm. area in twenty-three days, with complete destruction of an inoperable breast carcinoma. This patient was treated over a year ago and the skin, while showing unmistakable evidence of irradiation, is now soft and pliable and without any of the changes which suggest delayed trophic disturbances. Table 1 also shows the depth doses with comparable filters at higher voltages. With this heavy filtration our depth dose is approximately midway between that obtainable with 5 mm. copper filter and 400 constant potential at 75 cm. distance and the usual 200 kv. (peak).

In our treatment of abdominal carcinoma, where we are able to use three large fields, we may now obtain a tumor dose in excess of 4,000 r, an impossible depth dose at any practical distance with 0.5 mm. copper filtration. In fact, in treating small individuals over the thorax or abdomen and using three portals we have found that the depth dose has now become the limiting factor, rather than the skin dose.

Four cases serve to illustrate the possible uses of this increased filtration.

CASE REPORTS

CASE 1. M. S., female, white, aged fifty-one. History of sore mouth of two years' duration. Examination showed a fungating growth involving the entire lower left alveolar mucosa around the remaining teeth, the gutter and the lower half of the buccal mucosa. Biopsy showed squamous cell carcinoma, grade 1. There was a large hard submaxillary gland. Because of the extensive lesion, an oval area 11×15 cm. was treated including the primary lesion and gland. In twenty-four days this area received a total dose of 5,896 r, measured in air, at the daily rate of 268 r, Sundays excluded, with the

Fig. 1. Case 1. Height of reaction thirteen days after receiving 5,896 r to single area for buccal carcinoma with metastatic gland.

following factors: 220 kv. (peak), 20 ma., 30 cm. distance, 10 minutes, 1.25 mm. tin, 0.25 mm. copper, 1.0 mm. aluminum filtration. An intense epithelitis developed a few days before the treatment was concluded. The skin showed only a faint erythema at the end of treatment. The skin reaction reached its height on the thirteenth day, as shown in Figure 1, at which time the tumor had completely disappeared. The patient was able to eat with some difficulty and there was little pain. Nupercainal ointment controlled the burning. Figure 2 shows the extent of the healing on the thirty-fourth day after treatment. Figure 3 shows the extent of healing five months and five days after treatment. At this time there was an area of exposed bone around one of the remaining molars; the patient was having some pain but not of sufficient intensity to require medication. Figure 4 shows the skin completely healed nine months after treatment. The metastatic gland was not palpable. At the present time, fourteen months after treatment, the skin is smooth and soft. There is some increased pigmentation and some atrophy. There is absolutely no induration or edema. There is no

Fig. 2. Case 1. Extent of healing thirty-four days after treatment. Insufficient pain at any time to require internal medication.

Fig. 3. Case 1. Extent of healing five months after treatment. Primary malignancy and metastatic gland have disappeared.

evidence of malignancy in the mouth or in the glands.

This case is presented as an example in which a very radioresistant type of buccal carcinoma and its metastasis have been destroyed to date with the use of only external irradiation through a single portal. There are some minor skin changes but it is our contention that it would be impossible to reproduce this result with external roentgen rays with less filtration. We do not advocate the treatment of mouth lesions by external irradiation alone as was done in this case. We usually treat such cases by giving them about two-thirds this dose of external roentgen irradiation and treat the lesion locally with radium filtered through 1 mm. platinum. We believe this type of heavily filtered roentgen radiation is superior to external radium molds in the treatment of lesions about the head because the radiation is more easily directed to the lesion, the eyes are easily protected and there is always a uniform distribution of the radiation which is a difficult procedure with radium.

Fig. 4. Case 1. Skin shows some atrophy and increased pigmentation but no induration. Patient free of all evidence of malignancy for fourteen months.

Fig. 5. Case 11. Extensive epithelioma involving cartilage of ear and cheek. There was almost complete deafness of six months' duration.

Case 11. H. K., male, white, aged sixty-eight. History of an ulcerating tumor involving the right ear and cheek of two and a half years' duration. There was almost complete deafness in this ear of six months' duration. No previous treatment. Examination showed a typical epithelioma involving the entire ear, with erosion and destruction of the lower portion, and with extension on the cheek to the angle of the jaw (Figs. 5 and 6). Because of the involved cartilage and possible extension of the growth into the middle ear it was felt that the patient's best chance was with the selective type of irradiation from heavily filtered roentgen rays. In twenty days an area 7.5×9.5 cm. received a total of 6,800 r, measured in air, at the daily rate of 400 r, Sundays excluded, with the following factors: 220 kv. (peak), 20 ma., 25 cm. distance, 10 minutes, 1.25 mm. tin, 0.25 mm. copper, 1.0 mm. aluminum filtration. On the second day of treatment thirteen maggots were removed from the lesion. The reaction was mild and the patient had absolutely no pain at its

Fig. 6. Case II. Malignancy involved posterior surface of ear as well as anterior surface.

height two weeks after treatment. Three months after treatment the lesion was healed except for some exposed cartilage near the auditory canal, this exposed cartilage was removed by electrosurgery and the lesion healed in two months. The patient's hearing is perfect in this ear and there is no evidence of growth at the present time, one year after treatment (Figs. 7 and 8).

This case is presented to show how a badly infected epithelioma which had eroded and destroyed part of the cartilaginous portion of the ear and possibly had extended into the middle ear has apparently been destroyed. The fact that this result was obtained with less pain during and after treatment than before treatment according to the patient's own statement makes us feel that our best method of preserving the normal tissues is by heavy filtration. In our experience this method of treatment is superior to radium element needles or seeds because of the ease of application of a uniform dose to the entire field involved.

Fig. 7. Case II. One year after receiving 6,800 r to single area, heavily filtered roentgen radiation.

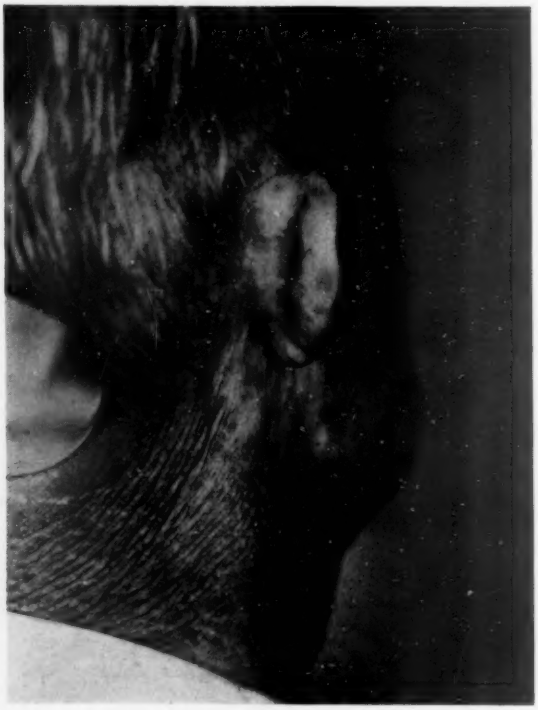

Fig. 8. Case II. Posterior surface of ear one year after treatment. Normal hearing has been restored.

Case III. R. G., male, white, aged twenty-eight.

History of removal of obstructing carcinoma from descending colon in November, 1932. Pathological diagnosis of adenocarcinoma of the sclerosing type. Two years later there developed a lemon-sized abdominal wall implant in the incision which was removed in December, 1934. Pathological report identical with the first report. Within two months patient developed another abdominal wall recurrence in the incision which apparently involved all layers and measured 10 cm. in diameter. Because of the rapid recurrence and size of the lesion the surgeon considered the case inoperable and referred the patient for roentgen

Fig. 9. Case III. Patient had an abdominal wall implant 10 cm. in diameter after surgical removal of adenocarcinoma of colon. Showing reaction from 4,500 r heavily filtered roentgen radiation ten days after treatment.

treatment. In a period of twenty-five days the patient received a total of 4,500 r to an area 20×20 cm., at the rate of 210 r daily, excluding Sundays, with the following factors: 220 kv. (peak), 20 ma., 35 cm. distance, 10 minutes, 1.25 mm. tin. 0.25 mm. copper, 1.0 mm. aluminum filtration. Figure 9 shows height of reaction ten days after treatment. Figure 10 shows beginning healing seventeen days after treatment. Figure 11 shows skin healed five months after treatment, and the tumor had entirely disappeared. Patient had no nausea during treatment and weight remained stationary. He is now working daily and is ap-

Fig. 10. Case III. Showing beginning healing seventeen days after treatment. Patient had no nausea or vomiting at any time and lost no weight.

parently free of disease, nine months after treatment.

This case is an example of good palliation, and possibly more, in a type of malignancy that we have in the past been considering hopeless. The skin is now smooth, soft and flexible.

Case IV. G. W., male, white, aged sixty-two.

History of perfect health until three months previously when patient developed epigastric pain and indigestion. He was placed on an ulcer diet without relief. During the next three months there was a los of 25 pounds in weight. No nausea or vomiting. There were black stools on several occasions. Roentgen examination of the stomach showed a large filling defect and

Fig. 11. Case III. Skin is smooth and soft and there is no evidence of recurrence nine months after treatment.

Fig. 12. Case IV. Inoperable carcinoma of stomach, showing ledge and filling defect on greater curvature near fundus. Patient received a tumor dose of 4,150 r without nausea or vomiting at any time.

ledge on the greater curvature characteristic of gastric malignancy. The location of the lesion made it inoperable and because of good results in 3 other cases of inoperable gastric malignancy (to be reported by one of us soon in this Journal) the patient was referred for roentgen therapy. Figure 12 shows the stomach before treatment. In a period of forty-two days the patient received 3,000 r, measured in air, to each of three areas, anterior stomach, lateral stomach and posterior stomach, or a total of 9,000 r. The technique was as follows: 220 kv. (peak), 20 ma., 50 cm. distance, 15×20 cm. field, 1.25 mm. tin, 0.25 mm. copper, 1.0 mm. aluminum filtration. Tke first treatment to each area was 100 r, the second treatment to each area was 200 r, the third and subsequent

Fig. 13. Case IV. Showing mild blistering of skin two weeks after receiving 3,000 r to each of three areas, anterior, lateral and posterior left upper abdomen.

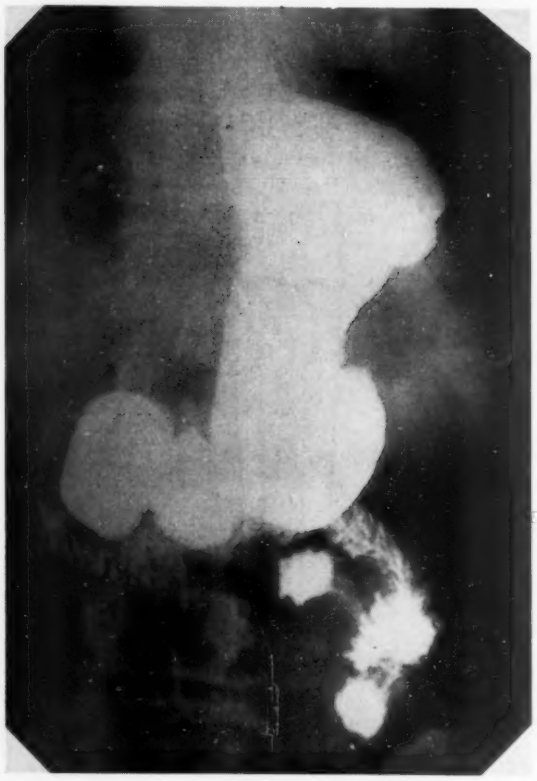

Fig. 14. Case IV. Three weeks after treatment all evidence of gastric malignancy has disappeared.

treatments were each 250 r (25 minutes). Only one area was treated daily and all areas were treated in rotation. We have found by experience in treating abdominal lesions that the nausea is lessened or avoided entirely if the daily dose is small at the beginning of treatment. The patient bore the treatments exceedingly well. There was no nausea or vomiting at any time and his appetite actually improved so that he was eating a full diet throughout the course of treatment and gained 4 pounds. Figure 13 shows the mild blistering skin reaction two weeks after treatment. Figure 14 shows

the stomach to be entirely normal three weeks after treatment and there was no roentgenoscopic evidence of malignancy. The tumor dose in this case was 4,150 r.

This case is presented to show that with this heavy filtration it is now possible to give a tumor dose in excess of 4,000 r to patients of average size. The most important lesson, however, is that we must completely change our ideas concerning the depth dose which the abdomen and epigastrium will tolerate safely. We have a patient with an inoperable carcinoma of the stomach, treated twenty-two months ago using 2 mm. copper filter, who received a tumor dose slightly less than this patient and is still free of disease and well. From our experience we believe that this modified Coutard type of therapy is applicable to every part of the body and an unknown number of inoperable malignancies of the liver, pancreas, stomach and intestines will now be brought within the possibility of a cure by roentgen irradiation.

CONCLUSIONS

A tin filter qualitatively equivalent to 5 mm. copper is described.

Greater use of filtration equivalent to 5 mm. copper at 220 kv. (peak) is advocated.

It is believed that there is a differential biological effect on skin and subcutaneous tissues dependent upon wave length.

With such filtration inoperable intra-abdominal malignancy is now brought into the field of radiotherapy.

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INDICATIONS FOR RADICAL SURGERY OF THE BREAST*

By HUGH AUCHINCLOSS, M.D.
NEW YORK CITY

WE ARE met today to compare notes and give one another help in the treatment of cancer of the breast. To discuss the indications for radical surgery and compare its merits with irradiation without emphasizing the most important factor of all—that factor which more than any one thing controls the success or failure of both of these methods of treatment, early recognition—would be a serious omission and I shall take the liberty, at the close of this paper, of offering a suggestion toward its accomplishment.

Certainly there are no indications for radical surgery if the disease has spread beyond those limits capable of being removed by operation.

This brings us, in any given case of cancer of the breast to our first duty—for it is not intended, in these few moments, to bring up the subject of diagnosis of cancer—i.e., doing all we can to find out whether the disease has spread beyond the recognized limits set for surgical removal.

Such a preliminary study should include symptoms that might indicate the presence of the disease elsewhere, information as to the probable duration of the disease and the rapidity of its growth, a painstaking physical examination of all parts of the body, carrying out obvious clinical tests, and finally, roentgen studies of the lungs, ribs, mediastinum, shoulder girdles, skull, spine, pelvis and the upper ends of both femora. Further roentgen studies of the gastrointestinal or other systems should be done only if indicated.

Failing to find evidence of metastatic disease by sign or symptom, one has to consider the local manifestation before deciding what to do. In spite of the fact that definite evidence of widespread invasion may be lacking, there are local conditions that allow of inferences that are well-nigh conclusive that the disease is out of control by surgery. These are not capable of being too clearly defined, but instances such as a rapid growth for several months in a young, well-nourished person with vigorous circulation and already existing, large, hard axillary nodes, or a lesion already fixed to, and involving the chest wall near the sternum, or one with much nipple involvement and widespread lymphedema, or one where many dilated veins and beginning skin ulceration are evident, these and a number of other combinations may lead one to infer that the case is not one for surgery.

Most remarkable surprises, however, in both directions, are in store for even the experienced, in prognosis. Cases that seem operable, show microscopical evidences of being relatively less malignant, and have no evidently involved nodes, may show persistences a few months after operation; apparently local, far-advanced cases may remain well many years.

In general, unless conclusive evidence exists that the disease has spread beyond where it can be removed at operation, the patient should be given the benefit of the doubt and operated on.

This is not the time to describe in detail what the "radical operation" is. Briefly, a radical operation should remove much skin, undermine closely and far, carry out what might be called a "fascial dissection," so that the chest wall, remaining muscles and axillary vessels and nerves are stripped clean, remove the pectoralis major and minor, except a few clavicular fibers of the major, and be closed by skin grafts, or perhaps an abdominal flap. It must be done meticulously, takes time and patience, is shocking and generally best fol-

* Read in a Symposium on Cancer of the Breast at the Twentieth Annual Meeting, American Radium Society, Atlantic City, N.J., June 10–11, 1935.

lowed by a transfusion. Entirely too many so-called "radical operations" are not "radical" enough.

It may seem strange for me to say it, but I can assure you I dislike the radical operation for breast cancer more than almost any operation I am called upon to do. I should like to give it up.

Our follow-up clinic, however, is bringing back to us a fairly encouraging number of cases, who had cancerous breasts removed from ten to twenty years ago. A few have lived over twenty years since operation and others are still alive whose history of onset dates back over twenty years. Some of these cases had metastases in the axillary nodes. I am sure the majority, if not all, of you will agree with me that most, if not all, of these patients, had they not had the operation would now be dead.

The point of it is, as your know already, a certain number of cases of cancer of the breast can remain clinically free of the disease for many years after the involved breast, with the immediate routes along which the disease spreads, has been removed.

Almost every worker in this subject begins with a genuine reverence for percentages and statistics of groups, usually not very large groups, of cases who have lived or died after the lapse of three to five years or longer.

Dr. Janet Lane-Claypon collected many of these lists for the English Ministry of Health and her collection is a model of its kind. These lists, however, are not about individuals and cancers that are all alike. Every individual on which such statistics are based is very different from the next; no two are alike. Such figures are based on so great a number of variants that their value is largely lost. Far more, I feel sure, can be learned through an intimate study of the extraordinary things that can happen in individual cases over long periods of time.

For the past twenty-five years it has been my opportunity to see rather intimately through many hundreds of visits made by patients through our follow-up clinic, cases treated by operation and irradiation, a relatively few cases treated by irradiation alone and still fewer cases given no treatment whatever.

I have, as have all of you, seen cases considered clinically hopeless, so helped by irradiation that suffering was relieved and even subsequent operation done. There was no evidence, however, that cancer had completely disappeared from the specimens removed.

So far, I have never yet seen a case of cancer of the breast, treated by irradiation alone, *remain* clinically free of the disease, or have it proved microscopically that the disease had been eradicated.

In a certain number of cases, by surgical operation, it has been possible to keep the patient clinically free from cancer for many years.

In a certain number of cases it has been possible to greatly benefit and apparently "cure" the patient by irradiation without removal of the diseased tissues, but I have never seen this proved. All the irradiated cancers of the breast subsequently removed have still shown cancer in the specimen.

For this reason, radical operation is still indicated in all cases where the disease cannot be demonstrated to have gone beyond the limits of surgical removal or where the evidence is not strong enough to warrant such an assumption. Otherwise, irradiation alone or irradiation followed by operation is indicated.

Postoperative irradiation in cases that have had a radical operation is, I think, of value. The decision as to what areas should be irradiated, either before or after operation, is one of interest and importance to surgeons and radiologists, especially the latter.

When cancer spreads from the breast we are wont to think first of its extension to the so-called axillary glands. This extension is too well known to dwell on and the arrangement of the lymph channels along

the long thoracic or external mammary vessels as they turn around the edge of the pectoralis major, with the fact that the axillary portion of the breast constitutes its greatest bulk and most frequently is the site of cancer, lend emphasis to this route. Grouping the brachial, axillary and subclavian nodes according to the main vascular channels they lie near is a convenient method for description. Lymph communication between the parietal, subpleural spaces and the nodes exists.

What other routes must be keep in mind? First, the lymph channels that go along the branches of the internal mammary artery. The breast receives most of its blood supply from those branches that perforate the second and third spaces preeminently. The internal mammary nodes that communicate with the retromanubrial nodes and the prepericardial nodes near the diaphragm receive much lymph from the breast. These, together with the lateral prepericardial nodes and vessels along the phrenic nerve have their tributaries from the diaphragm, the rectus sheath and muscle, the falciform ligament, and the right and left lobes of the liver. These anterior mediastinal vessels and nodes also receive the lymph from the vessels of the parietal, subpleural space.

In the second place, lymph channels from the breast enter the space between the external and internal intercostal muscles. These external, intercostal lymph vessels, though they communicate with the internal intercostal lymph vessels of the parietal, subpleural space, run backwards in contrast to the internal intercostal vessels, to enter the posterior intercostal lymph nodes in front of the necks of the ribs close to the spine. They are in the same fascial planes as the intercostal blood vessels.

In the third place, if we study the channels described by Rouviere and his associates, we shall find that the lymphatic vessels of the posterior two-thirds of the skull and scalp drain by means of the occipital and superficial parotid channels to a node or group of nodes anterior to the upper part of the internal jugular vein, thence backwards along the spinal accessory nerve to beneath the anterior edge of the trapezius and finally forwards along the transverse cervical vessels to glands in front of the junction of the internal jugular vein with the subclavian, into which branches from the subclavian lymphatics in their course to the right thoracic duct also empty. Whether this be the route from the axilla to the skull and scalp is not for me to say, but this route has been described with great care by Rouviere and offers a possible explanation for the frequently seen metastases in precisely these regions. Indeed, it is rare to see cancer of the breast spread along the deep cervical and jugular routes to the anterior regions of the neck or to the face.

Spread of cancer by retrograde or circuitous routes, once a lymph node or vessel has been thoroughly infiltrated, has been generally accepted by pathologists the world over. These potentialities have scarcely been enough appreciated by clinicians. It should receive far greater attention than it does. It explains many inexplicable problems in many diseases other than cancer.

May I call your attention to certain anatomical facts and leave with you the suggestion that they may explain some important clinical findings having to do with retrograde spread of breast cancer from the posterior intercostal nodes.

Let us bear in mind that these nodes and their tributaries correspond to the fascial plane in which run the intercostal vessels. Let us trace these vessels, for they serve as guides to the fascial planes that enclose them. Let us go farther, for the sake of argument, and assume that the lymph vessels we are studying continue alongside these vessels in these same planes. This, in other parts of the body, is true. Superficial lymph channels, beneath the skin, for instance, may run independently for some distance from the superficial veins. Once, however, they enter

nodes and become deep lymph channels, their course—for instance, the spermatic and ovarian channels in conspicuous fashion—are pre-eminently along the larger veins.

The twelve intercostal veins all enter the azygos system. All the veins from the dorsal and lumbar vertebrae enter the azygos system. Below the diaphragm the azygos veins are the ascending lumbar veins behind the psoas muscles. The iliolumbar veins and large communications from the internal iliac veins form the ascending lumbar veins. The gluteal and obturator veins enter the internal iliacs.

The fascial planes enclosing these veins are those investing the upper ends of the femora, the walls of the pelvis, the lumbar and dorsal vertebrae and the ribs and their intercostal spaces. Lymph nodes, vessels and plexuses correspond. These tissues are actually those too frequently found involved in breast cancer not to have some significance.

I would suggest that you bear this "azygos route" in mind in planning areas for irradiation.

In conclusion, early recognition of cancer anywhere is the sine qua non for successful treatment. We shall probably always have difficulty with deep-seated growths, but the breast is on the surface of the body where early recognition is possible, if the proper examination is made.

The laity is advised through educational campaigns to have periodic examinations, and if a lump is found by an individual she is advised to consult her doctor. Still the average breast cancer reaches the doctor unnecessarily late.

It is not so very unusual for a doctor to have to ask a woman to find the lump she has noticed, for him. He may have missed it entirely or be in doubt which of several slight areas of thickening it is. When she points it out, he feels it easily and is a bit chagrined that he did not find it first. In other words, a woman is capable of feeling lumps that even a doctor might not.

There is a way, and I believe only *one* way, to secure early recognition of cancer of the breast. Teach women to look for it themselves. Teach them when they are young to do this and tell them in such a way that they will not get frightened. This is the only way I know of, with our present knowledge, to reduce the tragic mortality of this disease. If they would do it, the mortality would drop at once.

This advice should be somewhat as follows: Teach every girl of twenty that, though cancer of the breast is a disease first manifested by a painless lump, most breast lumps are not cancer, and that every six weeks, i.e., eight times a year at least to feel the breast tissue when she wakes up in the morning. If she does feel a lump, she should see her doctor and get him to give her expert advice or refer her to some one who can.

Young people are not easily frightened and if they would follow this advice, the mortality rate from this disease would be appreciably decreased.*

* For discussion see page 388.

THE PLACE OF INTERSTITIAL IRRADIATION IN CANCER OF THE BREAST*

By ORVILLE N. MELAND, M.D., F.A.C.S.
LOS ANGELES, CALIFORNIA

THE aim of all treatment is curative if possible. In cancer of the breast this is theoretically attainable by radical surgical removal, but unfortunately this is only accomplished in the early case. When once the disease has passed from the organ itself to the first lymph node it has in fact already become a generalized condition. From a purely anatomic viewpoint, in cancer of the breast we should be dealing with a condition easy to cope with, as the organ is readily accessible to sight and palpation, but we are prone to disregard its physiologic connections. In reality, it is an accessory organ of reproduction intimately attuned to the vagaries of a multiplicity of endocrine disturbances which influence its activity. Consequently, these cellular changes induced during the rhythm of menstruation, pregnancy and lactation all profoundly influence the progress of the disease in its variable course. Furthermore, the organ itself is made up of such a loose texture of glandular, fatty and connective tissue that the disease once present may grow so rapidly and so insidiously that one cannot always make out any definite palpable mass nor can one be sure as to the exact location of its growing edge. All these facts have led not only to difficulty of recognition but also to the difficulty of total surgical removal without local recurrence. For these reasons many men, especially radiologists with a great deal of experience, have advocated the increasing use of radiation as a method of treatment. Such an opinion is based upon the beneficial effects seen and the results obtained in the inoperable group. Radiation may mean the use of either roentgen rays or radium.

In this presentation we are primarily interested in interstitial irradiation from platinum needles containing small amounts of radium. This is supplemented by preliminary roentgen irradiation to produce a more homogeneous effect. Our experience in its use extends over a six year period, and various phases have been previously presented by myself and associates.[2,6,7,10] For simplicity of analysis, the patients who have been treated are placed in five groups. The first four are really Steinthal groups, with an additional one representing a postoperative prophylactic group, as given below.

Group I (Steinthal I) Lump which may or may not be adherent to the skin.
Group II (Steinthal II) Lump with palpable, movable nodes in axilla.
Group III (Steinthal III) (a) Lump with nodes in axillary and supraclavicular regions. (b) Lump adherent to chest wall. (c) Lump with distant metastases.
Group IV (Steinthal IV) Postoperative recurrent group.
Group V Prophylactic group, where there has been a radical excision and where needles are inserted in axilla and other locations according to the Handley technique.

The following tables represent the patients treated, the dosage used, and the end-results. In looking over these tables one notes the frequent absence of pathological diagnosis. In the early patients, before using the aspiration method of biopsy, we did not insist on a pathological diagnosis, contenting ourselves with a clinical diagnosis which is reliable where metastases are already present, but which does not permit of reliable statistical analysis. In many of these patients the clinical diagnosis has been confirmed by the subsequent course, so that we consider this of sufficient reliability. Later we obtained

* Read in a Symposium on Cancer of the Breast at the Twentieth Annual Meeting, American Radium Society, Atlantic City, N. J., June 10–11, 1935.

TABLE I

GROUP I

No.	Year	Patient	Age	Size of Lesion Size of Breast	Pathological Diagnosis	Supplementary Treatment; X-ray	Radium Dosage †mg-hr.	Radium Dosage r	Present Condition
1	1931	N.	65	3 cm. Medium breast	None made	*B– 600 r A– 400 r S– 200 r	13,160.8	105,286.4	General condition good. Breast O.K. No palpable disease. 4 yr. 3 mo.
							9,660	77,280	
2	1931	T.	54	4 cm. Small breast	None made	B– 800 r A– 800 r S– 800 r	7,152	57,216	Reported to be dying from bony metastasis. 3 yr. 9 mo.
							Breast only treated		
3	1931	E.	62	Lump in breast removed 2 weeks ago and found to be carcinoma. Large breast	Adenocarcinoma	B– 500 r A– 500 r S– 500 r	10,037	80,296	Died from heart disease. Lived 1 year, 6 months. Breast normal.
							6,537	52,296	
4	1932	J.	46	5×6 cm. Large breast	None made	B–1,200 r A– 600 r	11,904	95,232	General condition good. Breast soft and normal. 3 yr. 2 mo.
							8,404	67,232	
5	1932	L.	59	4 cm. Medium breast	None made	B– 800 r A– 800 r	12,912	103,296	5/1/35—General condition good. Breast edematous, nipple firm. 3 yr. 4 mo.
							9,412	75,296	
6	1932	R.	52	3×3 cm. Medium breast	Adenocarcinoma Grade IV	B–1,200 r A– 400 r S– 400 r	12,821	102,568	Breast O.K.—soft, no disease palpable. Died, pulmonary metastasis. Lived 2 years.
							9,321	74,568	
7	1933	P.	52	2 cm. Medium breast; bleeding nipple	None made	B–1,000 r A– 800 r S– 800 r	10,675	85,400	Still clinically well but do not know condition of breast.
							7,175	57,400	
8	1933	A.	51	6×8 cm. Medium breast	None made	B–1,800 r A–1,000 r S–1,000 r	14,182	113,456	5/1/35—General condition good. Breast slightly edematous. No pathology palpable —2 yr. 2 mo.
							10,682	85,456	
9	1933	B.	75	4 cm. Large breast	Carcinoma	B–1,000 r A–1,000 r S–1,000 r	12,096	96,768	8/24/34—Lump remained which was removed and found to be only fibrous tissue. Died, heart failure, 10/12/34; 2 years.
							8,596	68,768	
10	1933	V.H.	66	2×2 cm. Large breast	Aspirated; adenocarcinoma	B–1,500 r A–1,000 r	11,996	95,968	Firm mass palpable. 5/20/35 —Mastectomy. Mass replaced fibrous tissue. Has new focus of carcinoma; 1 yr. 9 mo.
							8,496	67,968	
11	1933	L.	58	3×3 cm. Large breast	Aspiration not successful	B–1,600 r A– 800 r S– 800 r	12,595	100,760	Breast edematous. Area of fibrosis palpable. No other pathology; 1 yr. 8 mo.
							9,095	72,760	

* B–Breast; A–Axilla; S—Supraclavicular.

† Above line refers to total dosage breast and lymphatic areas. Below line refers to dosage in breast alone.

SUMMARY OF GROUP I

Living, clinically well, 4 years 3 months to 1 year 8 months, postoperative	7
Dead of cancer (lived 2 years after treatment)	1
Dead—intercurrent disease free from cancer clinically	2
Dying of cancer, 3 years 9 months after treatment	1
	11

tissues by the use of the Hoffman punch which confirmed our clinical suspicions; however, in some individuals this was at times unsuccessful.

DISCUSSION

A. Technique and Dosage. Interstitial irradiation is not a new procedure, but the method introduced by Keynes based

TABLE II

GROUP II

No.	Year	Patient	Age	Size of Lesion Size of Breast	Pathological Diagnosis	Supplementary Treatment; X-ray	Radium Dosage		Present Condition
							mg-hr.	r	
1	1929	K.	63	8 cm. Medium breast	None made	B– 600 r A– 600 r	15,180.2 11,680.2	121,441.6 93,441.6	Died 6/32—Metastasis to spine. Breast O.K., 4 years.
2	1930	B.	47	5 cm. Medium breast	None made	B– 200 r A– 200 r	17,874.6 14,374.6	142,996.8 114,996.8	5/1/35—Slight axillary induration. Breast O.K., 6 years.
3	1930	B.	72	6 cm. Large breast	Adenocarcinoma Grade III	None	12,791 8,291	102,328 66,528	1/30/32—Disease not controlled. Patient operated on, died coronary thrombosis 2 days postoperative. Patient lived 2 years after treatment.
4	1930	H.	55	6×7 cm. Small breast	None made	B–1,200 A– 600 r	13,824 10,324	110,592 82,592	Breast shows telangiectasia. Tender but no activity.
5	1930	B.	51	6 cm. Large breast	Adenocarcinoma Grade III	B– 600 r A– 400 r	16,329 12,829	130,637 102,632	5/1/35—O.K. Had breast removed and found to have carcinoma in it. Living 5 years.
6	1931	W.	47	6×5 cm. Medium breast	None made	B– 800 r A– 400 r	13,600 10,100	108,800 80,800	5/1/35—Marked telangiectasia. No tumor. Living, clinically well, 4 yr. 6 mo.
7	1931	T.	45	8 cm. Large breast	None made	B– 800 r	13,927 10,427	111,416 83,316	O.K. for 6 months. Moved to Mexico, lost track of.
8	1931	W.	63	8 cm. Axillary nodes Large breast			12,484 8,984	99,872 71,572	O.K. Feb., 1933—Mass gone, telangiectasia with tenderness. Moved away; lost track of after 1 yr. 6 mo.
9	1931	S.	77	6 cm. Small breast	None made	B– 600 r A– 600 r	10,886 7,386	87,088 59,088	Died 6/1/34—Spinal metastasis. Lived 4 years. Breast showed some fibrosis.
10	1931	E.	60	4×5 cm. Small breast	None made	B– 600 r A– 600 r	12,094 8,594	96,752 68,752	5/1/35—Breast O.K. Marked telangiectasis; 4 yr. 6 mo.
11	1931	D.	70	4 cm. Small breast	Squamous cell carcinoma	B– 400 r A– 400 r	5,165 3,965	41,320 31,720	5/1/35—Clinically well, 3 yr. 9 mo.
12	1931	R.	65	6×8 cm. Large breast	Adenocarcinoma Grade III	B– 400 r A– 400 r S– 200 r	12,940 9,440	103,520 75,520	5/1/35—Breast well except marked fibrosis; 4 years.
13	1932	B.	70	8 cm. Large breast	Aspiration not successful	B–1,700 r A–1,200 r	11,116 7,616	88,928 60,944	Edema of breast. 3 yr. 6 mo. No palpable masses. Some telangiectasia.
14	1932	C.	72	2×3 cm. Small breast	Adenocarcinoma Grade IV	B–1,000 r A–1,000 r S– 900 r	4,159 2,959	33,272 23,672	Died 10/11/32—Spinal metastasis, local extension. Dosage inadequate.
15	1932	W.	52	4×6 cm. Large breast	None made	B–1,200 r A– 800 r S– 400 r	14,464 10,964	115,712 87,712	Induration along axilla, otherwise O.K. 3 years.
16	1932	R.	72	4×4 cm. Axillary nodes Small breast	None made	B–1,000 r A– 600 r	12,912 9,412	103,296 75,296	Breast O.K. but died of spinal metastasis 12/1/34; lived 2 years.

TABLE II (GROUP II *continued*)

No.	Year	Patient	Age	Size of Lesion Size of Breast	Pathological Diagnosis	Supplementary Treatment; X-ray	Radium Dosage		Present Condition
							mg-hr.	r	
17	1932	LaF.	65	6×6cm Medium breast	None made	B– 900 r A– 900 r	15,754	126,064	5/2/35—O.K. 3 years. Breast soft.
							12,254	98,032	
18	1932	B.	73	5 cm. Medium breast	Adenocarcinoma Grade IV	B–2,100 r A– 450 r	10,176	81,408	3/28/33—O.K. Lost track of later.
							6,676	53,408	
19	1932	R.	46	6×8 cm. Medium breast	Aspiration not successful	B–1,700 r A–1,200 r	11,116	88,928	10/1/34—Died cerebral hemorrhage. Breast O.K. Lived 2 years.
							7,616	60,944	
20	1933	G.	75	6×8 cm. Large breast	Adenocarcinoma	B– 800 r A– 600 r S– 400 r	12,365	98,920	Died of coronary thrombosis 2 weeks after leaving hospital.
							8,865	70,920	
21	1933	H.	43	3 cm. removed for biopsy elsewhere. Medium breast	Adenocarcinoma	B–1,800 r A– 900 r S– 900 r	13,176	105,408	Marked fibrosis. O.K. otherwise. 2 years.
							9,676	77,408	
22	1933	D.	46	4×6 cm. Medium breast	Adneocarcinoma Grade III	B–2,000 r A–1,500 r S–1,000 r	15,681	125,448	Breast O.K.—Died spinal metastasis October, 1934. Lived 1 yr. 6 mo.
							3,181	25,448	
23	1933	McB.	79	8 cm. ulcerating. Medium breast	Adenocarcinoma Grade IV	B– 800 r A– 800 r S– 800 r	13,379	107,032	5/1/35—O.K. 2 yr. 2 mo.
							9,879	79,032	
24	1933	W.	60	4 cm. Small breast	Adenocarcinoma Grade III	B–1,200 r A–1,000 r	12,240	97,920	5/1/35—O.K. 2 years.
							8,740	69,900	
25	1933	S.	50	4 cm. Medium breast	Adenocarcinoma Grade IV	B–1,600 r A–1,000 r S–1,000 r	12,000	96,000	5/1/35—O.K. 2 years.
							8,500	68,000	
26	1933	C.	48	Nodule removed for biopsy. Medium breast	Adenocarcinoma	B–2,500 r A–1,000 r	10,941	87,528	3/28/35—O.K. except some edema. 1 yr. 6 mo.
							7,441	59,528	
27	1934	R.	57	5 cm. Medium breast	None made	Given in Germany. No accurate information	12,044	96,352	5/1/35—O.K. except fibrosis. 1 yr. 6 mo.
							8,544	68,352	
28	1934	C.	77	5 cm. Medium breast	None made	B–1,800 r A– 900 r	8,160	65,280	5/1/35—O.K. 1 yr. 6 mo.
29	1934	M.	34	6 cm. ulcerating. Medium breast	Adenocarcinoma Grade IV	B–2,400 r A–1,250 r S–1,000 r	13,410.6	107,284.8	5/1/35—O.K. Breast soft. 1 year.
							9,910.6	79,284.8	
30	1934	C.	74	8 cm.	None made	B–1,500 r	13,348	106,784	5/1/35—O.K. 1 year.
				Medium breast		A– 750 r			
							9,848	78,784	
31	1934	J.	46	5 cm. Medium breast	None made	B–1,000 r A–1,000 r S–1,000 r	14,169	113,352	5/1/35—O.K. 9 months.

SUMMARY OF GROUP II

Living free from clinical evidence of cancer, 6 years to 1 year.....19
Dead from cancer, all with spinal metastasis, 4 years to 1½ years..... 5
Dead—intercurrent: cardiovascular disease, 2 years to 2 weeks..... 3
Lost track of. O.K. clinically 6 months to 3 years after treatment..... 4
31

TABLE III

GROUP III

No.	Year	Patient	Age	Size of Lesion Size of Breast	Pathological Diagnosis	Supplementary Treatment X-ray	Radium Dosage mg-hr.	Radium Dosage r	Present Condition
1	1929	McN.	39	8×8 cm. Large breast; large axillary and supraclavicular nodes	None made	B– 400 r A– 400 r S– 400 r	18,408 14,908	147,264 119,264	9/30—Died, paroxysmal tachycardia. Breast still had palpable disease.
2	1930	D.	49	6×5 cm. fixed to chest. Large breast	None made	B– 600 r A– 200 r S– 200 r	13,792 10,292	110,336 82,336	11/3/34—Metastasis to supraclavicular nodes and shoulder girdle. 5/1/35—Recurrence—Living 5 years.
3	1930	E.	43	6×8 cm. fixed to chest. Large breast	Adenocarcinoma Grade III	B– 800 r A– 400 r S–2,200 r	12,360 8,860	98,880 70,880	3/5/35—Disease active.–Breast on the point of breaking down. Involvement of parasternal node. Breast removed. O.K. 5/1/35—5 years.
4	1931	C.	70	6×8 cm. Small breast, frozen to chest	Carcinoma	B– 600 r A– 400 r S– 400 r	11,093 7,593	88,744 60,744	5/1/35—O.K. 4 years. Breast deformed but soft.
5	1931	W.	54	8×5 cm. Ulcerating, fixed to chest. Medium breast	Adenocarcinoma Grade IV	B 500 r A– 400 r S– 400 r	14,472 10,972	115,776 87,776	Breast no palpable disease. Died 12/32 liver and spine metastasis. 1 year.
6	1932	W.	51	6×7 cm. Fixed to chest. Large breast	None made	B– 900 r A– 800 r S– 800 r	13,349 9,849	106,792 78,792	Breast O.K. Died 8/24/34 liver and lung metastasis. 2 yr. 6 mo.
7	1932	H.	61	2×3 cm. Movable Small breast. Supraclavicular node	Carcinoma	B–1,275 r	10,500 7,000	84,000 56,000	Breast O.K. Died liver carcinoma, autopsy—primary ? 8/28/34—2 yr. 6 mo.
8	1932	M.	64	6×8 cm. Fixed, small breast	Adenocarcinoma Grade II	B–1,600 r	10,032 6,532	80,256 52,256	Breast firm, fibrous. 5/1/35—Living with spinal metastasis. 3 yr. 2 mo.
9	1932	R.	74	13×12×6 cm. Frozen breast, fixed to chest	Adenocarcinoma Grade IV	B– 400 r A– 400 r S– 400 r	18,072 14,572	144,576 116,576	Died 9/14/32—Considerable improvement locally.
10	1932	S.	59	10 cm. Large breast. Axillary and supraclavicular nodes	None made	B–1,000 r A–1,000 r S–1,000 r	14,163 10,663	133,304 105,304	Breast no palpable disease. Lived 1 year. Died 10/30/33—Spinal metastasis.
11	1932	S.	55	6×7 cm. Fixed to chest. Small breast. Axillary nodes	None made	B– 800 r A– 800 r S– 800 r	6,720 5,520	53,760 44,160	7/12/34—Skin recurrence.–Dose too small. Has mitral stenosis and diabetes.
12	1932	V.R.	73	10×10 cm. Large breast, frozen to chest, ulcerating	Adenocarcinoma Grade IV	B–1,200 r A– 600 r S– 800 r	9,396 Breast on	75,168 ly needled	Died 6/7/33—Not much benefit from irradiation. Lived 6 months.
13	1933	M.	65	5 cm. Medium breast. Axillary and supraclavicular nodes	None made	B–1,500 r A–1,000 r S–1,000 r	12,212 8,712	97,696 69,696	Breast O.K. Still palpable supraclavicular node. Died 12/33, liver metastasis. Lived 1 year.
14	1933	H.	45	4 cm. Medium breast. Axillary and supraclavicular nodes	None made	B–1,600 r S–1,000 r	14,062 10,562	112,496 84,496	5/1/35—General condition good. Breast tender. Some telangiectasia present. Two years.

Table III (group III *continued*)

No.	Year	Patient	Age	Size of Lesion Size of Breast	Pathological Diagnosis	Supplementary Treatment X-ray	Radium Dosage mg-hr.	Radium Dosage r	Present condition
15	1934	B.	52	5 cm. Medium breast. Skin metastasis. Axillary node	Adenocarcinoma	B–1,600r A–1,000 r S–1,000 r	10,893 7,393	87,144 59,144	5/1/35—General condition good. Breast soft, no palpable disease. One year.
16	1934	D.	43	Mass removed left breast for biopsy. Masses right breast, bilateral axillary nodes	Adenocarcinoma Grade IV	(L)B–1,000 r A–1,000 r S–1,000 r	12,680 9,180	101,440 73,440	5/1/35—Clinically well. One year.
						(R)B–1,000 r A–1,000 r S– 600 r	1,920 1,420	15,360 11,360	

Summary of Group III

Living (free from disease) 4 years to 9 months	4
Living with disease—5 years to 3 years 2 months	4
Dead—intercurrent disease—9 months	1
Dead—cancer, 1 year to 2 years 6 months	7
No ulcerating or sloughing areas—all healed.	16

Table IV

group IV

No.	Year	Patient	Age	Size of Lesion Size of Breast	Pathological Diagnosis	Previous Treatment	Supplementary Treatment X-ray	Radium Dosage mg-hr.	Radium Dosage r	Present Condition
1	1931	R.	51	6×8 cm. Axillary fixed mass	Adenocarcinoma Grade IV	Local removal elsewhere 1 year ago	B– 600 r A– 600 r S– 600 r	9,564	76,512	Died brain metastasis 2 years after treatment.
2	1931	S.	47	Recurrent following local removal, axillary and supraclavicular nodes	Adenocarcinoma Grade IV	Mastectomy elsewhere 1 year ago	None given	12,042	96,336	6/1/35—Supraclavicular node still present. Has spinal metastasis. Breast O.K. Living 3 yr. 6 mo.
3	1933	H.	47	Recurrent both breasts following local removal. Small breasts. Blood from nipple. Axillary nodes	Carcinoma	Local removal elsewhere 1 year ago	(R)B– 800 r A– 800 r S– 800 r	7–956	63,648	6/1/35—O. K. two years.
							(L)B– 800 r A– 800 r S– 800 r	8,364	66,912	
4	1933	W.	70	Recurrent axillary, supraclavicular region and scar	Carcinoma	Radical operation elsewhere 10 years ago	X-Radiation given elsewhere—dosage not known.	7,324	58,592	5/1/35—Living, in good health, except for hypertension with some local evidence of disease; 2 yr. 6 mo.
5	1933	K.	66	Local recurrence following simple amputation	Carcinoma	Simple amputation elsewhere 2 years ago	B–1,000 r A– 200 r S– 200 r	4,529	36,232	Living, clinically well. Breast tender. No palpable pathology. Two years.
6	1933	H.	45	Local recurrence with axillary nodes	Adenocarcinoma	Simple removal lump 1 year ago	B–1,200 r A– 600 r S– 600 r	10,936	87,688	5/1/35—Living, good condition. Breast soft. Has spinal and supraclavicular metastasis; 1 yr. 6 mo.

Summary of Group IV

Dead from cancer	1	Lived 2 years.
Living—clinically well	2	1 and 2 years after treatment.
Living with cancer	3	2–2½–3½ years after treatment.
	6	

TABLE V

GROUP V

No.	Year	Patient	Age	Size of Lesion Size of Breast	Pathological Diagnosis	Treatment	Radium Dosage		Present Condition
							mg-hr.	r	
1	1929	L.	68	Medium breast; axillary nodes	Adenocarcinoma Grade IV	Radical removal ourselves	2,670	21,360	Died, 2 yr. 6 mo.; spinal metastasis. No local recurrence.
2	1930	H.	33	Large, fat breast. Axillary nodes	Inflammatory carcinoma	Radical removal elsewhere	1,676	13,408	Died Lived 2 yr. 6 mo. Metastasis to other breast. Quite comfortable.
3	1931	T.	37	Large breast. Axillary node	Carcinoma	Radical removal elsewhere	2,688	21,504	Living, 4 years. Clinically well.
4	1931	C.	69	Large breast. Large mass 8 cm.	Osteochondrosarcoma in fibroadenoma	Local removal ourselves. Refused radical operation	1,680	13,440	Living, 4 years. Clinically well.
5	1931	L.	49	Large breast. Axillary node	Carcinoma	Radical removal elsewhere	1,753	14,024	Died, 1 year. Local and distant recurrence.
6	1931	T.	54	Large breast. Axillary node	Carcinoma	Radical removal elsewhere	1,786	14,288	Died, 1 year. Local and distant recurrence.
7	1932	O'B.	33	Medium breast 8 cm.	Colloid carcinoma	Local removal elsewhere. Postoperative x-ray therapy 1,000 r	5,544 2,422	44,352 19,376	Died 5/1/35; general metastasis.

SUMMARY OF GROUP V

Dead of cancer.....5
Living, clinically well.....2 4 years each.
7

GENERAL SUMMARY

	Group I	Group II	Group III	Group IV	Group V	
Living and well	7	20	4	2	2	35
Died of carcinoma	1	5	7	2	5	20
Living with carcinoma	1	0	4	2	0	7
Died intercurrent disease	2	2	1	0	0	5
Free from carcinoma but lost track of	0	4	0	0	0	4
	11	31	16	6	7	71

on the experimental work of Regaud represents a new departure in this field. Our technique has been described on a number of occasions but is essentially that described by Keynes[4] in his early publications. To recapitulate, we surround the breast with one or more rows of needles, then insert them in the axilla, supraclavicular, infraclavicular and along the parasternal regions. Our needles have a filtration value of 0.5 mm. of platinum and they contain amounts of radium varying from 2 mg., 1.3 mg. and 1 mg. and their length varies from 4.8 to 3.6 cm. We question the value of inserting needles in the supraclavicular and parasternal regions as prophylactic measures but continue to do so. The dose as administered under ordi-

nary conditions is possibly inadequate, since one must use more needles when actual involvement is present if results are to be expected. For this reason we think the criticism by the late Mr. Birkett and Mr. Hutchison[3] is justifiable. The former advocated incision of the axilla and insertion of needles under finger guidance, while the latter uses greater quantities in both the axilla and supraclavicular regions and supplements his parasternal needles with radon implants. Undoubtedly this is a valuable suggestion. It is not to be wondered at that criticism should occur. It was thirty years from the time when Moore of Middlesex Hospital began to doubt the value of simple mastectomy until Halsted published his radical method of removal. Even now, valuable suggestions are made by surgeons toward the refinement of the Halsted-Meyer technique; so too must we expect changes from time to time in the technical procedure of interstitial irradiation, for comparison of end-results by various methods will determine the proper distribution of the foci of radiation. The ultimate aim of this therapy is to produce a massive irradiation effect in the breast and its lymphatic drainage areas through an extent slightly greater than that obtained by a radical Halsted operation. In fact we aim to produce a radium-Halsted of the breast.

Early in our work we were confronted with the question of dosage, which was purely empirical to start with. The needles were left in place from seven to thirteen days, depending on the size of the lesion. Keynes used 100 mg. and left his needles in situ seven days. Experience showed him that this resulted in little or no necrosis around the needles, and a satisfactory regression of the tumor took place with good lasting results. The amount of radium used in the individual case is of course dependent on the size of the breast, the size of the primary tumor and the presence or absence of metastasis in the lymph draining areas. In our series the average patient receives 3,500 mg-hr. in the lymph drainage areas, but in the breast itself it is different. It is perfectly obvious that a large breast will require more than a small one, while a tumor 8 cm. in diameter would need more than one of 3 cm. We have consistently tried to surround the primary lesion with one or more rows of needles, but we have also been forced to recognize that the remaining portions of the breast must be thoroughly irradiated if homogeneity is to be obtained. To assure ourselves of this we have made increasing use of a thorough course of high voltage roentgen therapy preliminary to interstitial irradiation. Cade,[1] one of the early workers in this field, recognized this by using a radium jacket three weeks after the needles were removed, a procedure which requires two periods of hospitalization, with increase of expense. For this reason we have used roentgen irradiation, which is an office procedure, with less cost to the individual. The dosage used in interstitial irradiation in the breast has varied from patient to patient; the average receives 8,000 to 9,000 mg-hr., but in one patient we gave 14,000 mg-hr. (Case 1, Group II), with no deleterious effects. The earliest attempts to arrive at a correct tissue dosage in breast cancer were made by Lee and Pack.[5] These workers used radon in gold tubes and based their dosage on the work of Quimby and Martin.[9] Their method of computation is based on the fact that it requires 10 erythema doses to kill squamous cell epithelioma, which means 2 mc. are needed for each cubic centimeter of tissue. Referring to Case 1, Group I, who had a mass 3 cm. in diameter, she received 9,660 mg-hr., while according to the Quimby-Martin calculations only 2,660 mg-hr. was needed. Likewise in Case 8, Group 1, who had a mass 6×8 cm. Using 8 cm. as the diameter, we find that she received 10,682 mg-hr., while the theoretical dosage should be 11,970 mc-hr. The application of the Quimby-Martin tables is not really possible in carcinoma of the breast since the needles are not inserted into the growth itself but rather

around the periphery of the growth which is supposed to assure an adequate radiation effect at the growing edge with enough crossfire at the center to destroy the tumor. Practically, the destruction of the cells in the center of the tumor is not always possible as is seen in Cases 1 and 5, Group II, Case 3, Group III, in which actively growing cancer was found in the hard mass that was a residue after thorough irradiation. However, such a distribution of needles does produce destruction of cancer in the center of a mass, as is noted in Case 9, Group I, where a hard mass remained which was removed and found to be only a fibrous mass free from cancer.

In the early part of this work we used little or no roentgen radiation but as time has gone on we have increased the roentgen radiation given to each patient. This, to our mind, leads to a more thorough irradiation effect throughout the breast, especially outside the outer row of needles where there may be foci of carcinoma unrecognized clinically. When combining both surface and interstitial irradiation we are confronted with the problem as to the proper time to insert the needles after roentgen radiation is given. Originally we waited three to six weeks after the last roentgen treatment was given; this gave us an idea as to the radiosensitivity of the lesion and enabled us to decrease the amount of interstitial irradiation. However recently we have begun to insert needles as soon as the patient recovers from the roentgen radiation effects in order to get a summation of radiation effect by the combined methods.

Breast carcinomas have been looked upon as belonging to the radioresistant group, in the majority of instances. To overcome this, radiologists have protracted and fractionated their treatments in order to increase the total dose with a diminution of skin effects. This is possible by giving 100 r daily over each of 2 portals to the breast and one each to the axilla and supraclavicular areas when a total of 2,000 r over each portal may be given in three weeks. Whether this dosage is sufficient is questionable; if we calculate our radium dosage in roentgens, as based on the work of Paterson and Parker,[8] we find that 1 mg. of radium filtered through 0.5 mm. of platinum gives off about 8 r per hour at 1 cm. distance. In interstitial irradiation this may not hold exactly true, as the tissue immediately around each needle receives more than this while the center of the tumor must receive considerably less. Nevertheless, it may serve as a basis of computation. It will be noted that in the column on radium dosage, besides the dosage in milligram-hours we have its equivalent in roentgens. Immediately one will see the enormous dosage obtainable. Even with this the disease is at times not controlled locally.

B. Effect on the Breast. After this type of treatment the breast undergoes various changes. When the acute effects, such as edema and radiodermatitis, have passed off, the breast may, after a few months, gradually assume the appearance of a normal breast. Sometimes a chronic edema with skin induration may persist over a long time—occasionally the breast appears normal but a bogginess may supervene. In these instances it is very difficult to be sure that there is not some cancer involving the subcutaneous lymphatics.

The breast may be exceedingly tender to the touch indefinitely. Any bump or injury may set up varying degrees of pain with resultant apprehension on the part of the patient, who naturally suspects return of activity. Ordinarily this tenderness disappears after a year. The skin is usually normal, sometimes it is thick and dry, at other times tanned. Some patients, especially blondes, have a very marked telangiectasia, which may appear a few months after the treatment is given or it may not be seen until two or three years have passed. The dosage used and the susceptibility of the individual patient are undoubtedly contributing factors.

The tumor mass in the breast recedes slowly. In the majority of instances the tumor completely disappears but then one also finds a residual palpable mass which,

in our experience, may or may not be the seat of carcinoma. Then it remains to be decided whether a mastectomy or a simple removal of the mass should be done. The clinical picture must be the basis of decision. It will be noted that we did not mention radical excision. We have attempted this on a few occasions and have been confronted by such an amount of fibrosis in the axilla that we have decided it is hazardous to do a clean dissection of the axilla without danger to the axillary structures. This is especially true when the endotherm is used, a method we use in all our breast surgery.

In all patients where there was ulceration, the breast healed and remained healed whether the patient lived or died subsequently of cancer. Except for one individual (Case 12, Group III) who had a very extensive involvement, no patient, whether she is living at present or died later from metastatic extension, went through the distressing effects of massive edema of the arm such as is seen after unsuccessful surgery or untreated disease. So from this standpoint the treatment has been remarkably effective as a palliative.

The question now arises as to which type of breast is suitable for interstitial irradiation. In the group of patients presented, none was rejected for treatment, whether the disease was extensive or whether the breast was large or small, provided the general condition of the patient was not obviously poor. The small, thin breast or the medium-sized breast is ideal as the insertion of the needles may be carried out with a fair degree of accuracy. In the large, fatty breast, which is usually pendulous, we have found that the accurate distribution of needles is impossible. There are bound to be areas in which dosage is small or at any rate inadequate. It was for this reason that we began supplementing our interstitial irradiation with surface roentgen irradiation to reach if possible the missed foci. Furthermore, the large fatty breast offers little chance for adequate tissue reaction with fibrosis that is so necessary for a successful outcome. We have come, therefore, to the conclusion that patients with a large, fatty breast should be treated by roentgen irradiation alone or by roentgen irradiation and surgery when ever possible.

Lymph nodes may disappear with no final palpable evidence of their previous presence; however, we have found that about twelve months after treatment some individuals may present an increasing thickness and firmness along the pectoral border. This seems to be a point of danger. In some this may represent a local recurrence, while in others it may be a delayed reaction involving the pectoral muscle itself. In a former publication, I made the statement that needles could be inserted with impunity into the muscle with no deleterious after-effects. Now, I am not so sure of this, for it results in fibrosis with diminution of motion on the part of the arm and pain on movement, but more important than this, it is impossible to rule out clinically the presence of activity in the lymphatics in this location. In 2 patients (Cases 2 and 15, Group II) such a condition arose, both were treated by roentgen irradiation and both improved and are apparently free from disease.

C. Causes of Death. There were a number of patients who died of intercurrent disease; we are not interested in the cause of death in these individuals except for the fact that in a few of them cancer was still present. On the other hand, we are interested in those who did die of cancer. We find that the local condition was controlled in all except 2 patients (Case 14, Group II and Case 12, Group III). The first of these had inadequate treatment while in the latter the disease was so extensive that no improvement could be expected. In all other patients, death was due to conditions they thought had no relation to the cancer, such as distant metastases to the brain, the lungs, the liver and the spine. The question naturally arises, did the implantation act as a precipitating cause of this dissemination? Such a thing is conceivable and may possibly be due to the manipulation incident to the operation. However,

the natural history of the disease is for it to spread into these same organs; consequently, this can only be decided by comparing its frequency in untreated or surgically treated controls. A striking feature, as was mentioned above, was that in all patients the breast was healed, there were no sloughing ulcers, no odor and in only 2 was there edema of the arm. This alone is worth remembering when comparing the treatment with the surgical group dying from recurrence.

Finally, is interstitial irradiation justifiable? This must be answered by referring to the individual groups. In the inoperable group there is no question as to its use. Its benefits to the patient, not only locally but generally, outweigh its disadvantages. In the recurrent group it may be used in conjunction with roentgen irradiation or surface radium. The extent of the disease will determine which method is better. In Group v we are not impressed with interstitial irradiation alone. It may be used but its scope is so limited that roentgen irradiation probably gives greater protection if surface irradiation is also given. In the operable groups, i and ii, there is place for argument. According to our present knowledge, in Group i where radical operation offers a 75 per cent chance for a five year clinical arrest, we think this should be the method of choice, especially if combined with preoperative roentgen irradiation. In Group ii, where the axillary nodes are already involved and the chances of a five year arrest vary from 15 to 30 per cent, interstitial irradiation may or may not be advocated. As a general rule, we think in the operable groups the use of interstitial irradiation is justifiable under the following conditions:

a. In selected cases when there is an acute inflammatory type of carcinoma after thorough external preliminary roentgen irradiation has been given.

b. When the patient is a young woman.

c. When the patient refuses operation.

d. When the patient is aged or has some complicating disease which makes the radical operation particularly hazardous.

CONCLUSIONS

The use of interstitial irradiation combined with surface irradiation is a very distinct advance in our treatment of cancer of the breast. It may be advocated in the inoperable group without hesitation; however, its use in the operable group is still open to question but it may be advised under certain conditions enumerated above. Radiation used in this way does definitely control the disease so that many of our patients have been clinically well as long as five years. As time goes on and experience accumulates, we should evolve a technique that will assure a homogeneous radiation effect comparable to the most carefully planned and executed Halsted operation.*

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* For discussion see page 388.

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THE EFFECT OF PREOPERATIVE IRRADIATION IN PRIMARY OPERABLE CANCER OF THE BREAST*

By FRANK E. ADAIR, M.D.
Attending Surgeon and Executive Officer, Memorial Hospital
NEW YORK CITY

CANCER of the breast is a disease which is treated universally by surgical means when possible. If the disease has gone beyond operable limits, radiation therapy is widely employed for palliation. In cases of advanced mammary cancer with distant metastases, irradiation occasionally works very effectively, especially in that group of cellular carcinomas where it causes destructive areas of the pelvis, femur or spine to be replaced by solid callus. Occasionally life is prolonged several years. In the advanced case, surgery is never considered, except for local relief or palliation, as, for example, with sloughing tissue.

We fully appreciate that the radical amputation is generally considered to be a fairly effective method of therapy in operable cancer of the breast. Having great respect for this confirmed viewpoint, we would hesitate to deviate very far from this position until we are on proven ground. However, we feel that we are justified in pursuing our preoperative irradiation studies because they are followed by the radical amputation, so that the patient's ultimate hope of cure is not lessened.

This study will confine itself to a consideration of *operable* breast cancer. By operable is meant that the disease is located in the breast, or even in both breast and axilla, but not beyond. Roentgen examination shows the chest negative for metastasis, and a careful consideration of symptoms rules out the probability of any distant metastasis. The operable case is the only type in which a complete cure is ever obtained. The results of surgical treatment in the outstanding American clinics vary but slightly if the classical radical amputation is meticulously carried out. It must, however, be admitted that there is a great difference among the radical amputations performed by different surgeons. Some do a hurried, careless, incomplete radical amputation, leaving much axillary fat and lymphoid tissue in situ, while others pay strict attention to the specific principles underlying this operation. The latter group rarely completes a radical amputation in less than two hours. They make a thorough investigation and removal of all axillary contents. It is necessary to remove both pectoral muscles in order to have free access to the entire length of the axilla.

If we consider the results of radical surgery in the hands of the best surgeons, we find (*a*) if the breast *only* is involved, approximately a 70 per cent five year cure is obtained; (*b*) if both the breast and axilla are involved, the five year cures are approximately 20 per cent. The two groups combined give approximately 35 per cent five year cures. These figures are taken as an average of the results of the best surgeons. The results of treatment by any type of therapy other than surgery *must* therefore be compared with these percentages. The cure percentage has changed but little during the past thirty-eight years, since the introduction of the radical amputation by Halsted. In fact, we doubt if anyone today obtains any better results than Halsted did. However, 35 per cent cure in operable mammary cancer is very far from satisfactory; and this fact impels us to pursue this problem further.

By the introduction of radiation, a welcome adjuvant was given surgery. Today high voltage postoperative irradiation has come to be employed by the majority of

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surgeons following radical amputation. Practically all studies indicate that postoperative irradiation adds definitely to the percentage of five year cures. Therapy at the Memorial Hospital, until two years ago, consisted of radical mastectomy followed by two high voltage roentgen-ray cycles. The results of this program gave 72 per cent five year cures when the disease was confined to the breast; 23 per cent when both the breast and axilla were involved, and 40.6 per cent for the two groups combined. This improvement over radical surgery alone should be credited to the added irradiation. Postoperative irradiation has now become widely accepted and seems to have fully justified itself. By so doing, it naturally has raised the question of the value of preoperative irradiation. If irradiation is effective in destroying residual cancer cells, after a radical operation, it would logically follow that irradiation should be of equal or of even more value when it is given as a preoperative measure. If one accepts this view, however, as a rationale of treatment, one must carefully consider several debatable points, namely:

1. If preoperative irradiation is effective, it is necessary to allow two months as a minimum after the completion of the treatments for irradiation to become fully effective in producing the desired tissue changes. The direct killing effect on the more sensitive cancer cells, together with the slower development of fibrosis and endarteritis and other results of irradiation, consumes a period of at least eight to ten weeks. Many clinicians will object to this delay, believing that the rate of tumor growth exceeds the rate of tumor starvation and strangulation secondary to irradiation. This view is understandable, but, in our study, it is obvious that the rate of tumor destruction far exceeded the rate of tumor growth, while the irradiation was being carried out. This period of delay therefore seems justified. We are fully cognizant of the opinions of some who believe that after a diagnosis of cancer is made, immediate operation is imperative.

2. Can the results of preoperative irradiation be considered as adding materially to the cure rate? Five year studies of a large number of cases so treated will answer this question.

3. Are the added difficulties of the operation following heavy preoperative irradiation, with the resultant wound complications, justified? They are if we obtain a very decided increase in our five year cure rate.

4. How far is it safe to go today in discarding the radical operation and substituting a complete irradiation program? Not until we have more information and obtain a higher percentage of cures will it be justified. Irradiation is making rapid and noteworthy strides each year and no one can now predict the best therapy ten years hence.

By the commonly accepted method of the radical operation followed by postoperative therapy, five year cures are obtained in 3 out of 4 cases if the disease is confined to the breast; and 1 in 4 cases only if the disease involves the axilla. Irradiation must produce better results than this, if an irradiation program is to supplant the radical operation and postoperative therapy. We recognize that there are cases complicated by tuberculosis, diabetes, syphilis, heart disease, etc., where surgery is contraindicated; and where irradiation is the only method available.

In the various European and American clinics there is today little serious effort being made to give preoperative irradiation to the operable cases. Dr. Coutard tells me that at the Curie Institute, in Paris, operable breast cancer is considered to belong to the realm of surgery. Regaud some time ago made the same statement. Morison of the London Cancer Hospital (Free) states likewise that their irradiation is confined to postoperative therapy and to treating the advanced inoperable cases by radiation. This same point of view is generally held in our American clinics.

Keynes of London treats operable breast

cancer by inserting radium needles into the breast tumor, parasternal spaces, axilla, infraclavicular and supraclavicular spaces. He is the only one, with whose work I am familiar, who has entirely supplanted surgery by interstitial irradiation. He told me recently that he obtains more success in treating the axilla by his method than he does by treating the breast. Recognizing that the axillary space occupies a wide area, extending from the lateral chest wall to the sternoclavicular joint, across which pass the large axillary vein and its many tributaries, it is difficult for me to understand how Keynes so accurately places his radium needles as to be more effective in the axilla than in the breast itself. It is understandable how, by his method of irradiation of the axilla, there might be an added safety factor when combined with external irradiation, but he rarely employs external irradiation. Careful microscopic studies should be made on a series of his cases so treated following a radical amputation. We will then know exactly the accomplishments of his method.

In 1933, I reported our results of radiation therapy, using interstitial and external irradiation as the complete method of treatment.[1] We found in the 47 cases so treated that there was 23 (49 per cent) five year survivals when the disease was confined to the breast. (This is to be compared with the 72 per cent five year survivals when surgery combined with postoperative irradiation was employed). In the operable cases involving both the breast and axilla there was not one five year cure. However, in the light of modern irradiation, it is known that these patients did not receive a sufficient amount; furthermore, many were treated with low voltage roentgen rays. Our results were in marked contrast to those of Keynes, who finds it easier to cure the axillary disease than the breast. As he has not yet reported five year cures on his work, we must withhold judgment on the effectiveness of his method.

It is usually conceded that the axilla offers the most difficult problem presented in the treatment of breast cancer. It is true for two reasons: first, the extent of this irregularly shaped space, and second, the response to treatment of cancer-invaded axillary nodes, scattered through bulky adipose tissue, is entirely different from the response of cancer tissue located in a vascular organ, such as the breast.

The problem offered in the treatment of cancer of the breast differs with each pathologic type, as well as each anatomic type of breast. The problem of treating a localized adenocarcinoma 2 cm. in diameter is obviously entirely different from that presented by a diffuse duct cancer which fills a large portion of the mammary duct system. The anatomy of the tumor is entirely different.

A small grade 3 infiltrating cancer, whose metastatic deposits have filled the axillary chain of nodes, again presents a special problem having little in common with the other types mentioned above. The treatment of a small breast, snug against the chest wall, presents an entirely different problem in radiation therapy from the long pendulous breast reaching to the umbilicus. In other words, the treatment of breast cancer is not *one* problem, but *many* problems.

Two years ago we started treatment of a series of operable breast cases giving preoperative irradiation by the fractionated dose method (Coutard). Approximately two to three months after the completion of the irradiation cycle, a radical amputation was done, and careful microscopic studies made of the residual cicatrix or cancer, as the case may have been. This study has given us much information on dosage, technique, time factor, viability of the cancer cells, general effects on the body as a whole, etc. The study has proved so illuminating that we are impelled to pursue it further. Before ideal results can be reached, techniques must be further changed; time factors altered; more specific attention given to the individual variations of the particular case; clinical cancer types more

sharply recognized; interstitial irradiation more commonly employed as an adjunct in those types resistant to external irradiation. A great many factors must be altered.

This research here presented shows that one group of mammary cancer cases, the operable, heretofore generally held to be a surgical problem only, may now be considered also a problem for the radiologist.

In this study of preoperative irradiation effects, it must be stated in the beginning that in every instance there was a positive biopsy report of cancer of the breast. We recognize that there are those who consider that aspiration biopsy material is not as satisfactory as biopsy material obtained by incisional methods. However, we make no apologies for this form of biopsy so freely used in our institution. It is a method satisfactory to our pathologists—Dr. Ewing and Dr. Stewart. Its interpretation requires special study and great experience along these lines. In the hands of the competent, this method is steadily gaining in general acceptance.

Without this method of biopsy, it would have been impossible to make this study, first, because physicians will not accept the clinical diagnosis of others on a case of cancer; secondly, and especially, because the recent scar of the incisional biopsy breaks down under the heavy radiation delivered making such full irradiation impossible. Aspiration biopsy is therefore an important step in the work here reported.

Our study is based on 117 cases of operable mammary cancer. Each case had (1) positive biopsy; (2) preoperative irradiation; (3) followed two or three months later by (4) a radical mastectomy and (5) careful tissue studies. Of this number 65 cases were treated through five portals by the fractionated dose method, using the 200 kv. roentgen machine, giving 300 r daily to each of two portals. Fifty-one cases were treated similarly using the 4 gram radium element pack and giving 8,000 mc-hr. to one portal per day. The portals used in both series were one tangential to the breast medially and one tangential to the breast laterally, thus cross-firing the breast lesion from two directions. The axilla was cross-fired through three ports: (*a*) axilla and supraclavicular anteriorly, (*b*) axilla direct, (*c*) axilla and supraclavicular posteriorly.

In our studies made and recorded on the patient's chart the day of the operation, the clinical results of therapy were tabulated thus: (1) breast tumor same size; (2) breast tumor reduced in size; (3) residual thickening only; (4) breast tumor entirely gone. Of the 18 cases treated by roentgen radiation giving 1,800 r per portal, there was not one instance in which the tumor remained the same size as originally described. In other words, irradiation, if given in fairly large doses, practically always causes reduction of the size of the tumor in varying amounts, depending on the type of pathological process present. Anaplastic carcinoma usually completely disappears, while colloid carcinoma changes very little in size. Of these 18 cases clinically examined, there was reduction in size or disappearance of the tumor in all cases (Table I).

Table I

Eighteen cases treated by roentgen radiation, each portal receiving 1,800 r. Clinical changes in the size of the breast cancer

	Number of Cases	Percentage
Tumor same size	0	0
Tumor reduced in size	4	22
Residual thickening only	8	44
Tumor entirely gone	6	33.3

Similar results were obtained by using the radium pack on the breast and axillary nodes.

Of the 36 cases treated by giving 1,200 r per portal, 43 per cent had complete *clinical* disappearance of axillary nodes. In contrast to this, 18 cases were treated giving 1,800 r per portal. With this treatment 55 per cent had complete *clinical* disappearance of the nodes (Table II).

Table II

BEHAVIOR OF ENLARGED AXILLARY NODES UNDER ROENTGEN TREATMENT

	Complete Clinical Disappearance	No Clinical Changes	Reduction
Cases given 1,200 r per portal	43%	40%	17%
Cases given 1,800 r per portal	55%	33%	11%

These results show that by increasing the dosage 600 r per portal, we obtained 12 per cent more *clinical* disappearance of nodes. In connection with the studies on the axillary contents, it was frequently noted that there was a great diminution in volume as well as marked atrophy of the lymphatic tissue. It must be concluded that heavy irradiation is responsible for (*a*) a softening of the lymphatic nodes; (*b*) a definite diminution of volume, and (*c*) in some instances, complete disappearance of nodes. It does not follow, however, that, in axillary contents where a complete clinical disappearance of a bulky mass has occurred, there will of necessity be no disease found. It is a very common occurrence to have a bulky metastatic mass greatly diminish or even completely disappear clinically. Although the clinical examination reveals these reductions and disappearances, this in no accurate way coincides with the microscopic finding in the laboratory.

Irradiation greatly softens the breast tumor so that at times it becomes extremely difficult for the clinician to be sure that any tumor remains. The characteristic hardness of the cancer entirely disappears so that the breast seems of the same consistence throughout.

When the amputated breast is examined in the laboratory, the pathologist has a new and difficult problem locating the tumor or its residual scar. It usually becomes necessary to locate the original site of the tumor by cutting the breast in small parallel slices. Dr. Ewing and Dr. Stewart frequently locate the original site in difficult cases by noting (*a*) a sclerosed hyalinized area, (*b*) a puckered scar, or (*c*) a few yellowish streaks. The consistence of this area is soft and differs entirely from untreated carcinoma of the breast. A section taken from this type of material sometimes shows no residual cancer; at other times only a few clusters of atrophic degenerating cancer cells so badly damaged that their viability is in great doubt; while, on the other hand, the microscopic study may reveal fully stainable and possibly viable cancer cells. It is difficult for the pathologist to be correct on his gross study of the breast material and the axillary contents. Gross and microscopic tissue studies require that one have experience in this special field of irradiated tissue.

In the microscopic study of 39 cases picked at random, it was found that the gross description of the axillary contents was incorrect in 10 cases (25 per cent). This emphasizes the great difficulty of correctly interpreting the gross presence of cancer in heavily irradiated lymphoid tissue. The errors occurred always in the same direction, namely, in stating that a node was negative for the presence of cancer when microscopically it was later found to be involved.

The time period of treatment is of equal importance with the amount of irradiation given. The factors of distance, filter, the number of roentgens per treatment, time interval between treatments, time allowance between completion of treatments and operation, skin target distance, etc., are each a matter for further study. In our cases the time between the delivery of the last preoperative radiation treatment and the operation, varied widely. The shortest interval was twelve days; the longest 300 days, and the average sixty-six days.

Cases Treated by High Voltage Roentgen Rays. Of the 65 cases treated preoperatively by roentgen rays, 13 were between thirty

and forty years of age; 25 between forty and fifty years; 20 between fifty and sixty years; and 7 between sixty and sixty-five years. No case over sixty-five years of age is included in this series.

Thirty-six patients were given 1,200 r to each of five portals; 11 patients, 1,500 r per portal; and 18 patients, 1,800 r per portal (Table III). For the sake of convenience in studying this irradiated material, we have devised a scale of radiation effects.[2] This scale of radiation effects is the following:

R.E.B.: Indicates the radiation effect in the breast tumor; R.E.N. indicates the radiation effect in the axillary nodes.

R.E.B. 0: Signifies that irradiation destruction is most incomplete and has been minimum. It may signify that there was complete destruction in one area with persistence of viable disease in another area.

R.E.B. 1: Signifies the minimum effects of irradiation, such as atrophy, cell hydrops and slight sclerosis.

R.E.B. 2: Signifies a more marked condition but similar to R.E.B. 1.

R.E.B. 3: Signifies that the process of tumor tissue destruction has been extremely marked, and that there is a question whether the tumor cells are viable. It will remain for the element of time to prove whether this R.E.B. 3 group is capable of regeneration or metastasis. Dr. Ewing is of the impression that the cases falling into this group may eventually be completely cured and incapable of recurrence. We are taking the position, at least for the present, that this group may be capable of recurrence.

R.E.B. 4: Signifies that after a most careful study has been made of tissue taken from many portions of the breast, there is no sign of cancer.

We have made similar studies on the axillary nodes. Their irradiation classification scale would be R.E.N. 0; R.E.N. 1; R.E.N. 2; R.E.N. 3; R.E.N. 4.

The degree of radiation effects on each group of cases treated is tabulated (Table III) for both the breast and axillary contents.

A glance at Table III shows that of the 36 cases treated by 1,200 r per portal, 19 per cent had complete *microscopic* disappearance of the breast cancer; not *clinical* disappearance as discussed above. When the dose was increased to 1,800 r per portal (600 r more per portal) the complete microscopic disappearance nearly doubled—namely, 33.3 per cent. In a similar way the radiation effects (R.E.B. 3) went from 14 to 28 per cent. Of the total 65 cases treated by roentgen radiation, in 14, or 21.5 per cent, the tumor disappeared completely from the breast.

Unfortunately, the success of cancer destruction in involved axillary nodes is in marked contrast to that of the breast. In only 3 (8 per cent) of the 39 cases with involved nodes, treated by roentgen rays, was there complete microscopic disappearance. Of these 3 cases, 2 occurred where the patient received 1,800 r per portal. The crux of the problem in treating mammary cancer is the axilla. Slightly more than half the cases, 51 per cent, have axillary involvement. External irradiation, as delivered by our technique, is not a great success in curing axillary nodes.

Skin Damage. In every one of the 65 cases treated by roentgen radiation, the skin was in good condition for operation at the end of four to eight weeks. Roentgen irradiation produced in a large proportion of the cases a marked desquamation and blistering of the skin of the axilla, breast and submammary regions. The skin is usually more damaged where perspiration produces excess moisture. It is possible to give more radiation in the winter months than the summer months and, on account of this fact, at times it becomes necessary to reduce the amount of radiation planned, especially during hot weather. In many instances patients during this time must come for daily dressings. Our patients are forewarned that blistering and superficial skin destruction may occur. This is accomplished by giving them a paper stating this fact on their first hospital visit.

Our study shows that the secretion from these denuded areas is strongly acid (litmus paper test). The patients suffer much pain

TABLE III

MICROSCOPIC STUDIES

SHOWING NUMBER OF CASES TREATED BY EACH METHOD WITH RESULTANT RADIATION EFFECTS

Treatment by 200 kv. x-rays	Breast Cancer R.E.B.					Cases with Axillary Involvement	Cases without Axillary Involvement	Axillary Disease R.E.N.				
	0	1	2	3	4			0	1	2	3	4
1,200 r per portal Five portals 50 cm. S.T.D. 36 cases	15 41%	5	4	5 14%	7 19%	23	13	13 65%	6	1	2 9%	1 4%
1,500 r per portal 11 cases	5 45%	2	0	3 27%	1 9%	7	4	4	2	0	1 14%	0 0%
1,800 r per portal 18 cases	6	0	1	5 28%	6 33%	9	9	5	1	1	0 0%	2 22%
Total cases 65	26	7	5	13 20%	14 21.5%	39	26	22	9	2	3 7%	3 8%
Treatment by 4 gram radium element pack 6 cm. S.T.D.												
20,000 mc-hr. per portal 15 cases	6 40%	4	1	2 13%	2 14%	6	9	5 83%	1	0	0 0%	0 0%
24,000 mc-hr. per portal 37 cases	7 20%	6	5	6 16%	13 35%	15	22	9 60%	1	0	3 20%	2 13%
Total cases 52	13	10	6	8 15%	15 30%	21	31	14	2	0	3 14%	2 9%
Grand total cases 117	39	17	11	21 15%	29 25%	60 51%	57	36	11	2	6 10%	5 8%

and sleeplessness during the two to three weeks when the skin is at the height of its reaction. We advise the patient to take two showers daily. This washes away the painful acid secretion. Following this, a mildly alkaline salve is applied which should contain a small amount of scarlet red to stimulate epithelial regeneration. No non-irritating application, so far as we know, has yet been produced for the diminution of skin moisture.

Cases Treated by the 4 Gram Radium Element Pack. There were 52 cases treated by the radium pack, using the same portals for this treatment as for the roentgen irradiation. The distance of the pack from the skin was 6 cm., with a 6 cm. diameter of the pack opening, producing approximately a 10 cm. diameter circular portal at the skin surface. In 15 cases, 20,000 mc-hr. per portal was employed. Of these 15 cases, in only 2 (14 per cent) did we obtain a complete microscopic disappearance of the tumor from the breast; and in *none* of the 6 cases having axillary involvement was there microscopic disappearance of disease.

Thirty-seven cases were treated giving 24,000 mc-hr. per portal; and of this number 13 cases (35 per cent) had complete

microscopic disappearance of the breast tumor, which is more than double the figgure (14 per cent) produced by giving 20,000 mc-hr. per portal. Of the 15 cases with axillary involvement, treated by 24,000 mc-hr. per portal, the nodes were sterilized in two instances (13 per cent) (see Table III).

The technical difficulty of treating the axilla by the radium element pack is chiefly that the portals are entirely too small for large subjects. It sometimes becomes necessary to add another portal anteriorly to cover the axilla completely, and in this case it is difficult to keep from overlapping the skin.

Comparison. We have been attempting to make a fair comparison of the two instruments—the 200 kv. roentgen machine and the 4 gram radium element pack. During the past two years, the number of roentgens given per portal has been repeatedly changed as has also the number of millicurie-hours delivered per portal by the radium pack. It now seems from our microscopic tissue studies that 1,800 r per portal compares very closely in tissue effectiveness with the radium pack treatments, giving 24,000 mc-hr. per portal (see Table IV).

There is one distressing complication which has presented itself in those cases treated by large doses of the radium element pack, giving 8,000 mc-hr. daily, namely, persistent skin ulceration. Of 37 cases treated giving 24,000 mc-hr. per portal, 20 cases (54 per cent) had persistent radionecrosis. Such ulceration is particularly painful. This condition persists where there was previous cross-firing of the breast portals. This is an important point against the use of such heavy doses given daily by the radium pack; however, it seems necessary to give such large doses in order to accomplish a 35 per cent microscopic disappearance of the breast cancer. It suggests that radiation is applied too quickly by this technique. Through this ulcerated area, bacteria enter the lymphatic routes to the axilla, so that wound complication is a common occurrence. The cases treated by roentgen rays, on the other hand, even though there were many instances of marked temporary skin damage, all healed without persistent ulceration; and accomplished about the same amount (33 per cent) of complete destruction in the breast cancer (see Table III). When it comes to the treatment of involved axillary nodes, the roentgen rays seemed definitely a superior instrument, as there was complete microscopic disappearance of the axillary cancer in 22 per cent of the cases treated by the roentgen rays, while there was but 13 per cent destruction in those nodes treated by the radium pack (see Table IV). The radium pack is a very effective instrument but the length of the axilla demands a larger portal than is given by the pack.

Table IV

SHOWING PERCENTAGES OF COMPLETE MICROSCOPIC DISAPPEARANCE

	Breast	Axilla
1,800 r per portal	33%	22%
24,000 mc-hr. per portal	35%	13%

We well know by microscopic studies that irradiation cures by two methods: first, by the direct killing effect on cells that are radiosensitive, and secondly, by an imprisonment process on the part of the surrounding tumor bed which results in cutting down the blood supply and laying down a dense fibrous wall—in other words, by starvation and imprisonment. The second process is cancer retardation and control, a process strongly emphasized by Ewing in the Mutter Lecture. Cancer control and cure by irradiation requires a long period. It is possible for stainable cancer cells to remain in situ for a great many years without dissemination. Before the New York Surgical Society in 1931, I reported 3 cases in which biopsy revealed the presence of carcinoma cells six and a half years after the patients first received irradiation.[3] It is therefore highly probable that those radiation effects in which

R.E.B. 4 (see Table III) was reported do not represent the total benefit of irradiation. If it were possible to add the R.E.B. 3 and R.E.B. 4 effects, the beneficial results of radiation treatment would be very impressive. Time will be required to estimate the true value of preoperative irradiation. My prediction, however, is that such heavy irradiation should add materially to the five year cures.

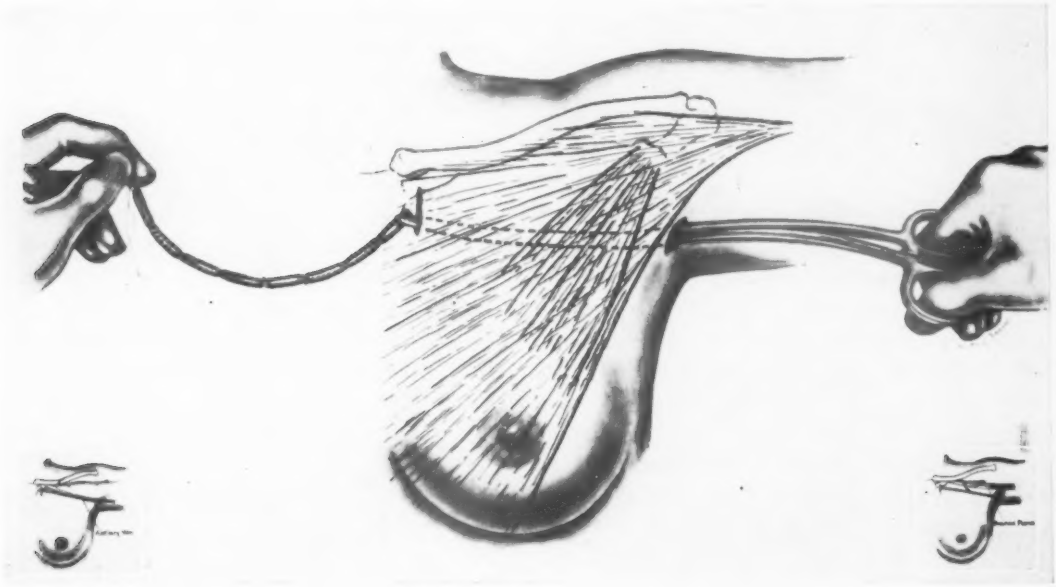

FIG. 1. Showing the axillary radium tandem. The operator is ready to draw the end of the tandem through the skin near the sternoclavicular junction, on through the pectoralis major muscle (clavicular portion), behind it and the pectoralis minor muscle, laying the tandem parallel to and near the axillary vein. The tandem consists of a rubber catheter containing five radium capsules. The tandem remains in situ until a 2,000 mc-hr. dose is given.

Axillary Tandem. Due to the fact that external irradiation alone is not sufficiently effective in treating involved axillary nodes, we devised an axillary radium tandem (Fig. 1) to be placed across the axilla under novocaine anesthesia.[2] Our hopes are that this addition to axillary irradiation will be of value. We have used this tandem in 40 cases which will be the basis of a later report on this subject.

Sterilization. In any consideration of therapy for breast cancer, the subject of sterilization of the ovaries today occupies a position of great interest and discussion. During each menstrual period, the follicular output from the ovaries has a profound effect on the duct tissue of the breast which is manifested by (*a*) marked proliferation in the duct cells; (*b*) lengthening of the ducts; (*c*) multiplication of the acini. The effect is not only on the normal lining cells, but many think also on the abnormal mammary cells—the cancer cells. The effect of menstruation is widely conceded to have a very deleterious effect on the young woman with breast cancer. In our clinic we urge the young patient to subject herself to irradiation sterilization of the ovaries, especially if she is pregnant at the time, has had a recent pregnancy, or is under thirty-five years of age. It is a question how far this viewpoint can be judiciously urged, and we are watching with intense interest other clinics where these studies are being made. An acute menopause in the young woman entails much mental and physical suffering and should be carried out only after careful consideration.

Radiation Pneumonitis. As increasingly

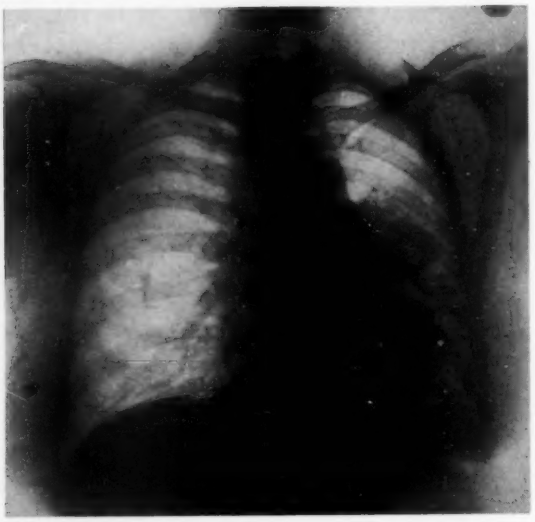

Fig. 2. Localized pneumonitis following irradiation. A chest film showing the localized or segmental type of lung involvement. This patient's chest was negative for any abnormality before commencing high voltage roentgen treatments; biopsy was positive for breast cancer; no evidence of any active disease present after four years; no pulmonary symptoms.

greater doses of radiation have been applied, a new complication has manifested itself—radiation pneumonitis. This complication was first pointed out by Groover, Christie and Merritt[4] in 1922. It has since been observed and described by several radiologists. One of the most careful of the many studies on the subject is that by McIntosh,[5] who with L'Esperance had the rare good fortune to study autopsy material. Both Holfelder and Finzi have emphasized the importance of the tangential technique in order to avoid lung damage. It is difficult, however, to escape this complication entirely, especially in the cross-firing of the axilla. We wish to mildly disagree with Kaplan[6] who states: "In our opinion technical errors account for such occurrences." We are sure that as the doses increase, more instances of deep pulmonary damage will be manifest.

We do not venture an opinion as to etiology aside from the large doses of deep roentgen radiation. It occurs at all ages. It seems that a pre-existing bronchitis is not a contributing cause. In our cases it has occurred more frequently in the younger age groups, possibly because we are more apt to insist that the young subjects receive heavy irradiation.

In our cases treated by the radium pack there were no clinical cases of pneumonitis; this was also true in the cases receiving 1,200 r per portal. However, as the roentgen-ray dosage increased, several cases presented this damage. The clinical signs are cough, dyspnea, pain through the chest, and a tendency to a dusky color, characteristic of poor aeration of the lungs. There are two types shown by the roentgenograms. In one type, there is a segmental or localized area of diffuse thickening radiating outward to the periphery from the mediastinum (Fig. 2). The second type shows a more extensive area of thickening involving almost the entire lung. The heart is retracted to the affected side, the diaphragm is elevated and there seems to be general fibrosis and thickening of the entire area (Fig. 3).

In some instances the clinical symptoms

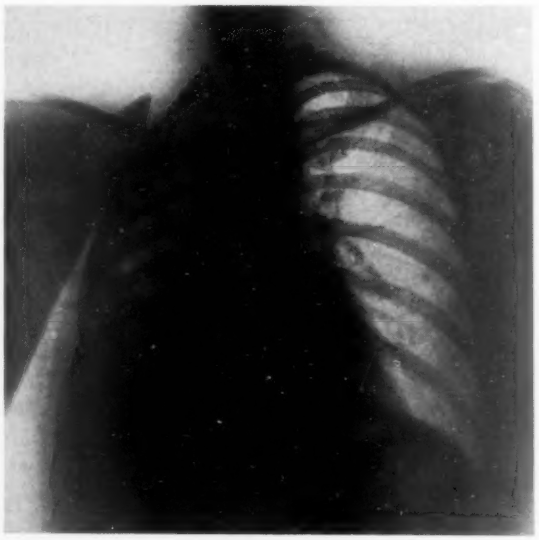

Fig. 3. Extensive pneumonitis following irradiation. A chest roentgenogram showing the more extensive type of radiation pneumonitis. The lung on the affected side is the seat of generalized thickening, fibrosis and contraction. The diaphragm is elevated; the heart retracted to this side. Entire side is smaller and capable of less expansion than the opposite side.

persist for many weeks before the patient begins to improve. The interpretation of the film is most difficult and uncertain. It will take careful study of such autopsy material to correctly interpret and differentiate (*a*) metastatic disease; (*b*) pulmonitis, and (*c*) treated metastatic cancer of the lungs.

Kaplan is at least stimulating in insisting on this complication as a technical error, because it will make all more eager to avoid pneumonitis. On the other hand, we feel that this complication will become a more frequent occurrence as doses become greater.

Anemia. There is a complication which we have noted in a few instances which is of the gravest importance, namely, secondary anemia. We have been unable to ascertain any cause for the secondary anemia in our few operable cases which had it. There was no metastasis to the bones to account for it. We surmise that the low hemoglobin which has been at about 80 per cent, or lower, may be due to irradiation of areas over large blood volumes, such as the mediastinum and neck. It is a warning which must be heeded and carefully guarded against.

Pneumonitis and secondary anemia are complications which tax the ingenuity and resourcefulness of the one who technically applies radiation.

SUMMARY

1. In the Memorial Hospital, radical surgery followed by postoperative irradiation produces 72 per cent five year cures when the breast alone is involved; 23 per cent when both the breast and axilla are involved. The two groups combined give 40.6 per cent.

2. Our results using both external and interstitial irradiation as a *complete therapy* have been reported[1]. We obtained 48 per cent five year cures when the carcinoma was confined to the breast; this is in contrast to the results obtained by radical surgery and postoperative irradiation, namely, 72 per cent. We obtained no five year cures by our method in cases having axillary involvement; this is in contrast to the cases treated by radical surgery and postoperative roentgen irradiation, which gave 23 per cent five year cures.

3. It is pointed out that each anatomic variety and each different histological type present a special problem to the therapist. Proper treatment is not one problem but many problems.

4. A study was made on 117 operable cases of breast cancer, each having a biopsy positive for cancer. Observations were made both clinically and microscopically to note the effect of preoperative irradiation. Sixty-five cases were treated by the 200 kv. roentgen machine, and 52 cases by the 4 gram radium element pack.

5. In all instances, irradiation caused clinical reduction in the volume of the breast tumor. To a lesser extent this was true of the axillary disease. The tumor tissue softens and commonly takes on the same consistence as the mammary tissue.

6. It requires a pathologist with experience in the special field of irradiated tissue to interpret the gross appearance correctly, and even then there is a good proportion of mistaken gross interpretations.

7. A scale of radiation effects is recorded so that effects may be better compared with each other.

8. Table III shows the treatment delivered to each group of cases, with the resultant radiation effects. Sixty-five cases were treated by roentgen rays using 200 kv.; of these, 36 cases were given 1,200 r per portal, with a complete microscopic disappearance from the breast in 19 per cent of the cases and from the nodes in 4 per cent. Another group was similarly treated giving 1,800 r per portal; this group gave a 33 per cent microscopic disappearance of the cancer from the breast and 22 per cent from the axillary nodes.

9. Fifty-two cases were treated by the 4 gram radium element pack. Those treated by 20,000 mc-hr. per portal had 14 per cent complete microscopic disappearance of the tumor from the breast; and

no instance of complete tumor disappearance from the axilla. The group treated by 24,000 mc-hr. per portal obtained a 35 per cent disappearance of the tumor from the breast and 13 per cent from the axilla.

10. Microscopic tissue studies show that cases receiving 1,800 r per portal correspond very closely in tissue effectiveness to radium pack doses of 24,000 mc-hr. per portal. These comparisons also seem to reveal no biological differences in the two types of radiation effects. The same type of microscopic effect is delivered by the roentgen ray as by the radium, and it is not possible for us to distinguish microscopically which type of therapy has been employed.

11. In the cases receiving 24,000 mc-hr. per portal by the radium pack, distressing skin ulceration persisted at the time of operation in 54 per cent of our cases. It suggests that this technique is not satisfactory because it is too caustic where there is overlapping of the two breast portals.

12. Additional axillary irradiation is described. A tandem containing five radium capsules is placed across the axilla behind the pectoral muscles to aid in more effectively irradiating the axillary space.

13. Sterilization of the ovaries in pregnant women who have carcinoma of the breast is advised; also in all women under thirty-five years of age.

14. The complications of radiation pneumonitis and secondary anemia are considered. These complications suggest that every effort should be made to give, as far as is practical, tangential irradiation to avoid them.*

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* For discussion see page 388.

THE TREATMENT OF INOPERABLE, RECURRENT AND METASTATIC CARCINOMA OF THE BREAST*

By EUGENE T. LEDDY, M.D., *and* ARTHUR U. DESJARDINS, M.D.
Section on Therapeutic Radiology, The Mayo Clinic
ROCHESTER, MINNESOTA

THIS paper is based on a study of 573 patients who had inoperable, recurrent or metastatic carcinoma of the breast and who were treated in the Section on Therapeutic Radiology at The Mayo Clinic in the years 1924 to 1933, inclusive. Table I gives the yearly incidence and classification of these cases. Tables II and III serve to illustrate the well-known facts that, in the great majority of cases, carcinoma of the breast affects women who are in "the cancer age," that is, from forty to sixty-five years of age, and that the lesion may involve either breast with about equal frequency. From a casual survey of the histories of these patients, we have been unable to obtain any information about the relationship of lactation to the development of carcinoma of the breast, but it might be stated, incidentally, that many of these patients never had been pregnant, and that in 4 of the cases in this group, the patients were men. Trauma, infection of the breast, or lumps, which had been present in the breast for a long time, did not

TABLE I

INCIDENCE AND CLASSIFICATION OF CARCINOMA OF BREAST

Year	Cases	Nature of lesion			
		Inoperable	Recurrent	Metastatic	Combined recurrent and metastatic
1924	43	6	25	4	8
1925	56	12	27	7	10
1926	49	17	23	7	2
1927	52	9	35	4	4
1928	61	17	33	7	4
1929	53	14	33	5	1
1930	48	9	27	7	5
1931	92	12	35	24	21
1932	62	13	12	15	22
1933	57	13	18	14	12
Total	573	122	268	94	89

TABLE II

AGE OF PATIENTS WITH CARCINOMA OF BREAST

Year	Cases	Age of patients, years					
		Less than 30	31 to 40	41 to 50	51 to 60	61 to 70	More than 70
1924	43	0	4	20	15	3	1
1925	56	1	20	14	16	4	1
1926	49	2	4	15	21	4	3
1927	52	1	11	14	17	7	2
1928	61	2	8	18	20	12	1
1929	53	0	10	19	16	6	2
1930	48	0	6	19	18	4	1
1931	92	2	17	37	23	11	2
1932	62	0	10	22	20	10	0
1933	57	—	7	26	11	10	3
Total	573	8	97	204	177	71	16

TABLE III

BREAST INVOLVED IN CASES OF CARCINOMA

Year	Site of involvement		
	Right breast	Left breast	Both breasts
1924	24	17	2
1925	31	23	0
1926	25	23	1
1927	28	23	1
1928	24	36	1
1929	24	28	1
1930	21	27	0
1931	42	46	4
1932	31	32	1
1933	22	32	3
Total	272	287	14

* Read in a Symposium on Cancer of the Breast at the Twentieth Annual Meeting, American Radium Society, Atlantic City, N.J., June 10–11, 1935.

TABLE IV

DURATION OF TUMOR BEFORE TREATMENT AT THE CLINIC*

Year	Duration, years																	Earliest duration
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16 to 23	Not given†	
1924	17	13	2	3	2	1	1	2		1	1							
1925	23	14	5	5	2		1	1				1		2			2	1 week
1926	18	6	2	3	1			1									18	3 weeks
1927	19	12	4	1			1										15	1 month
1928	22	9	4				1										25	
1929	17	5	4	1	1	1			1								23	3 weeks
1930	19	3	3	2												1 (18 years)	20	1 month
1931	36	21	2	1	1		1			2		1				1 (21 years)	26	1 month
1932	11	16	4	3	1							1	1		1		24	2 days
1933	17	17	10	3		4	2		1			1	1			1 (23 years)		
Total	199	116	40	22	8	6	7	4	2	3	1	4	2	2	1	3	153	

* Before patient sought treatment at the Clinic. This often was impossible to establish.
† Especially in inoperable group.

occur with sufficient frequency to impress themselves on us as important etiologic factors. From the present study we have nothing to contribute toward the solution of the etiology of this very common disease.

As can be seen from Table IV, more than half of the patients had had carcinoma of the breast for more than a year before they came to the Clinic for treatment. The chronicity of the lesion is most pronounced in the group of cases in which the carcinoma was inoperable; this is shown in Tables V and VI. It seems likely that, in many of the cases in which the carcinoma reached the stage of inoperability in three months or less, the patients gave an inaccurate history of the onset of their lesions. It is unfortunate that, in the group in which the carcinomas were inoperable, neither the apparent acuteness nor chronic-

TABLE V

INOPERABLE CARCINOMA OF BREAST: DURATION BEFORE AND AFTER TREATMENT AT CLINIC

Year	Duration before treatment						Duration of treatment			Duration after treatment					No note
	Months		Years				Months		Years	Months		Years			
	3	6	1	2	3	4	1 to 3	6	1	3	6	1	2	4	
1924	1	1	2	1		1	4	2		2		2		1	1
1925	1	2	7		2		6	6			3	2	4		3
1926	4	3	4	1	2	3	13	2	2	1	1	1	1	2	9
1927	1	2	1	3	1	1	7		2			1	1		7
1928	1	3	4	7	1	1	12	5		2	3	1	3		8
1929	2	5	3	4			14				1	3	3	1	6
1930	2	4	2			1	6	2	1		3	1	1		4
1931	2	3	2	1	1	3	6	6		1	1	5			5
1932		2	9	1	1		10	3		1	1	2	4		5
1933	1	4	3	1	2	2	9	2	2		2	1	3		7

ity of the tumors was checked by a microscopic examination to correlate the apparent and actual degrees of their malignancy. If the figures for duration of the tumors can be taken at their face value they serve to emphasize the point made by many authors that the clinical malignancy and life history of carcinoma of the breast vary widely, and at the same time they bring to mind the necessity for caution and conservatism in evaluating the results of any form of treatment. From our study, it seems as if the most malignant form of carcinoma of the breast, that which most rapidly becomes inoperable and hopeless, is the form which begins in pregnancy, or which shortly antedates it, an observation which already has been made by Harrington[1] in his study of carcinoma of the breast.

At this point it might be advantageous to define the criteria by which these cases are grouped. By "inoperable carcinoma of the breast," we mean carcinoma which, in the opinion of the consulting surgeon, was beyond surgical intervention. This state includes, in general, ulcerated carcinoma, carcinoma fixed to the thoracic wall, carcinoma with widespread cutaneous metastasis, carcinoma which could be extirpated surgically but which was accompanied by involvement of supraclavicular lymph nodes, carcinoma with extensive involvement of the axillary and supraclavicular lymph nodes, carcinoma with osseous and visceral metastasis irrespective of involvement of the lymph nodes, and carcinoma that was associated with some organic disease, which made the risk of operation too great. In many cases, these criteria were not sharply drawn; it occasionally happened that in the face of some of these conditions, in the opinion of the surgeon, operation still had much to offer the patient as a palliative measure.

We regard "recurrence" as the postoperative appearance of carcinoma in the field of operation.

TABLE VI

INOPERABLE CARCINOMA OF BREAST: SHORTEST AND LONGEST DURATION BEFORE AND AFTER TREATMENT AT CLINIC

Year	Shortest duration		Longest duration		Total life
	Before treatment	After treatment	Before treatment	After treatment	
1924	2½ months	1 month	6½ years	3 years	
1925	2 weeks	1 month	3 years	2 years	
1926	1 month	1 month	8 years	1-7/10 years	10 years
1927	6 months	1 month	7 years	2 years	
1928	1 week	2 months	7 years	2 years	7 years
1929	3 weeks	8 months	9 years	5 years	14 years
1930	6 weeks		4 years	2 years	4½ years
1931	4 months	5 months	12 years	2 years	12 years
1932	5 months	11 days	3 years	2 years	5 years
1933	3 months	3 weeks	4 years	1½ years	4 years

For our purposes "metastasis" is definable as the spread of carcinoma, from the breast, to structures of the body which were not involved in the operation.

INOPERABLE CARCINOMA OF THE BREAST

In 122 of the cases in this series, the carcinoma was inoperable.

In the treatment of inoperable carcinoma of the breast, we have followed the general principles which we previously have advocated in our consideration of the method of multiple converging beams.[2,3] As time passes, we are more and more convinced of the efficacy of this technique, which has proved superior to all other methods of irradiation that we have tried. We are not in a position to say whether the insertion of radium needles or the protracted ap-

TABLE VII

EFFECTIVENESS OF ROENTGEN TREATMENT OF INOPERABLE CARCINOMA OF THE BREAST

Year	Total number cases	Less than three treatments (1 or 2)		More than three treatments	
		Improved	Unimproved	Improved	Unimproved
1924	6	0	4	2	0
1925	12	1	5	6	0
1926	17	2	11	3	1
1927	9	0	7	2	0
1928	17	2	10	3	2
1929	14	2	12	0	0
1930	9	0	6	3	0
1931	12	0	6	6	0
1932	13	4	6	2	1
1933	13	0	9	4	0

plication of roentgen rays has any advantage over the method of multiple converging beams, as we have not used either of the former methods to any extent. However, from a review of the literature on the results of treatment of this lesion, there seems to be no valid reason to urge us to make any radical change in our present method.

In the majority of cases in which the carcinoma was inoperable, only palliative treatment could be employed (Table VII). In 87 of the 122 cases in which the carcinoma was inoperable, the patients received less than three courses of roentgen irradiation, an amount, which, in our experience, has been insufficient to produce worth while or lasting benefit. Of the 87 patients who, according to our standard, received incomplete or insufficient treatment, 76 were unimproved. Undoubtedly, some of these patients might just as well have been left untreated, while others received treatment in name only. When the results in the cases in which the patients received insufficient treatment are compared with the results in the cases in which the patients received three or more courses of irradiation, it becomes evident that if a patient is to be treated with roentgen rays as a palliative measure she should receive at least three courses of treatment.

Forty-two patients, or approximately a third of all those who were treated, improved. This improvement was manifested by healing of an ulcer in 16 cases, by disappearance of cutaneous metastasis in 5 cases, and by cessation of hemorrhage and discharge in 21 cases. This improvement has lasted for more than two years in a few cases, but, owing to the extent of the disease and the systemic damage from it, no patient has lived and remained well clinically for five years, which is usually accepted as a criterion for "cure." We feel that because treatment with multiple converging beams is tolerated well by most patients, and inasmuch as the results which have been obtained with this method are better than those which have been obtained with any method that we have tried, its continued use is indicated.

Since the duration of inoperable carcinoma of the breast may vary from a few weeks, to ten, or more, years (as is evidenced by Table V), one must be very conservative in estimating the value of roentgen therapy as a life-prolonging procedure. As a palliative measure, its value seems self-evident.

TABLE VIII

PRIMARY TREATMENT AND DIAGNOSIS IN CASES OF RECURRENT CARCINOMA OF THE BREAST

Year	Treatment			Diagnosis
	Excision of tumor or simple amputation of breast	Palliative operation	Paste	Benign tumor
1924	16		2	
1925	17		2	
1926	8	1	2	1
1927	18		1	
1928	14		2	1
1929	19			
1930	18		1	
1931	25		1	5
1932	13		2	
1933	16		3	
Total	164	1	16	8

RECURRENT CARCINOMA OF THE BREAST

Recurrence of carcinoma took place in 268 of the cases in this series. As one reviews the histories of these cases, one is immediately struck by the frequency with which incomplete, or at least nonradical, operation had been performed (Table VIII). In view of the fact that radical surgical operation has been the universally accepted method of treatment for carcinoma of the breast for many years, it is surprising that so many surgeons throughout this country had chosen a minor operation as the primary procedure. In 164 of the cases in which the carcinoma had recurred, excision of the tumor or simple amputation of the breast was all that was attempted at operation. In 8 of the cases in this group, in which the carcinoma was proved by the postoperative developments, a diagnosis of benign tumor had been made. In 16 cases in the recurrent group, some form of nonoperative treatment, such as escharotic pastes, had been employed. We concur with Harrington in the opinion that the most unsatisfactory results follow radical operation after some previous minor surgical procedure, and we feel that this view holds true as well for radiotherapy as it does for operation. Table IX, which includes cases of recurrent and metastatic carcinoma, exemplifies the fact that the incidence of return of the disease is lower after radical operation than it is after any minor procedure.

Since it is not our purpose to attempt to establish the value of roentgen therapy after operation, we are unable to state the percentage of cases in which recurrence or metastasis followed operations which were performed at the Clinic. In the majority of these cases, the patients received varying amounts of roentgen therapy. In practically all of the cases which were seen in the later years of this study, the patients received what we regard as complete postoperative roentgen irradiation. The data are quite inadequate to allow one to form a worth while opinion about the value of radiotherapy given elsewhere.

TABLE IX

NATURE OF PRIMARY OPERATION IN CASES OF RECURRENT AND METASTATIC CARCINOMA OF BREAST

Year	Operation at the Clinic		Operation Elsewhere	
	Simple	Radical	Simple	Radical
1924	0	8	25	5
1925	0	11	22	11
1926	1 (palliative)	9	14	10
1927	0	8	23	12
1928	1 (palliative)	6	25	13
1929	0	7	24	9
1930	0	9	23	10
1931	0	54*	26	10
1932	0	24†	23	7
1933	1	22§	25	10
Total	3	158	230	97

* Seven of these were palliative.
† Four of these were palliative.
§ Two of these were palliative.

Regardless of the kind or amount of treatment employed, the majority of the patients had a return of the disease within two years after operation (Table X). Since by far the greater number of all patients had both recurrence and metastasis, we have made no attempt to differentiate the two types of lesions, but have combined them in this table. It is remarkable to note that in 46 cases the lesions recurred after the five year period. It also seems to us that, in the 59 cases in which recurrence or metastasis developed within three months after operation, the carcinoma must have been inoperable at the time of operation. With such extremes in the time of recurrence and metastasis as those we have found, it seems fair to say that only by studying large groups of cases can surgical or radiation treatment be evaluated correctly, so that natural variations in the duration of malignancy will not vitiate the conclusions that may be drawn.

We agree in general with the view that early radical operation is the most satisfactory procedure to employ in the treat-

TABLE X

RECURRENCE OR METASTASIS OF CARCINOMA OF BREAST AFTER OPERATION

Year	Present at operation	Months after operation			Years after operation												
		1	3	6	1	2	3	4	5	6	8	10	11	12	13	15	21
1924	1	1	7	4	6	4	2	2	2	1	2	2	1				
1925		1	7	7	12	5	2	1	1		4		3				
1926	1		2	5	7	4		5	3	1	1	2					
1927	2		3	5	19	6	4	1		1		2					
1928	1	3	4	11	7	11	4	1	1							1	
1929	1	1	9	7	9	7		1			3						
1930			4	7	11	4	5	1	2			9					1
1931	12	1	5	15	19	13	7	4	2								
1932	3	1	6	8	11	10	6	1				1		1	1	1	
1933	6		4	3	17	11	4			4	1	1		1	1		
Total	27	8	51	72	108	75	34	17	11	7	11	17	4	2	2	2	1

ment of carcinoma of the breast. Although some studies of carefully selected cases indicate that some form of radiotherapy may be substituted for radical operation, there are no data available, as far as we know, which compare the incidence of metastasis or recurrence in patients who have been treated by the different radiotherapeutic methods alone.

Similarly, this group of cases does not permit deductions about the value of preoperative irradiation. In several cases in this study, the patients received preoperative treatment with radium or roentgen rays, at the Clinic or elsewhere.

That the involvement of the axillary lymph nodes at operation is a bad prognostic sign is universally recognized. The extent of axillary involvement and the grade of malignancy according to the method of Broders are the two best criteria by which the status of a given case can be established. Patients without axillary involvement but with a high degree of malignancy have a doubtful prognosis. This is illustrated by Table XI, which shows the

TABLE XI

GRADE OF MALIGNANCY OF CARCINOMA OF BREAST WITHOUT INVOLVEMENT OF AXILLARY LYMPH NODES

Year	Grade 1	Total cases	Grade 2	Total cases	Grade 3	Total cases	Grade 4	Total cases	Not graded	Total cases
1924	0	0	0	0	1	3	0	8	3	5
1925		0	1	2	0	3	0	8	2	4
1926		0	0	0	0	4	0	7	3	7
1927	Skin nodes only	1	0	3	0	4	1	9	1	4
1928		0	1	1	1	3	1	0	1	5
1929	0	0	0	1	0	6	0	11	0	1
1930		0	0	0		6	1	18	1	1
1931		0	1	2	5	23	3	34	2	3
1932	0	0	0	0	3	8	1	22	0	1
1933		0	2	2	1	10	1	17	1	1
Total	1	1	5	11	11	70	8	134	14	32

incidence of recurrence and metastasis in cases in which operation was performed at the Clinic. Attention might be drawn to the fact that in these cases the grade of malignancy was generally high.

Table XII shows the same thing from another point of view. This table includes cases in which a radical surgical procedure was performed, as well as those in which only a lymph node was excised for histologic study. One might predict, after consideration of the high incidence of tumors graded 3 or 4, that the results of treatment

TABLE XII

GRADE OF CARCINOMA, REGARDLESS OF SITUATION

Year	Grade 1	Grade 2	Grade 3	Grade 4	Not graded
1924	1		4	9	2
1925		2	3	12	0
1926			6	10	2
1927	1	3	5	10	2
1928		1	5	13	0
1929		1	6	12	0
1930			7	18	0
1931		2	24	35	1
1932			8	22	1
1933		2	10	17	1
Total	2	11	78	158	9

of the recurrent and metastatic group of tumors would in no sense be outstanding.

From an analysis of the results of radiotherapy in this group of cases, we can find no definite relationship between radiosensitivity and the index of malignancy, although, on general principles, considering the type of cell in question, one would expect tumors of grade 4 to be the most responsive. However, it is fair to state that the general physical condition of many of the patients had been lowered to such an extent by the malignant disease that their power of regeneration was too low to react to any stimulus to repair.

TREATMENT OF RECURRENT CARCINOMA OF THE BREAST

If the nodules of recurrent carcinoma are few in number and localized in a small region of skin of the chest the easiest and most certain method of eliminating them is surgical excision with either the knife or the cautery. Postoperative irradiation is indicated on general principles. It should be said, however, that the evidence that such postoperative radiation treatment will postpone further recurrence is meager, for not infrequently recurrence has followed. This fact probably is evidence that the "resistance" of the body to carcinoma was at a very low ebb.

If, on the other hand, the recurrence in the skin is extensive and would have to be dealt with by wide excision to the extent that closure might be difficult, or if the recurrent nodules are widely scattered, probably the most effective treatment is radiotherapy. Whether this should be carried out with radium or with the roentgen rays depends, in general, on the extent of the disease and the amount of radium available. With the facilities for radiotherapy which we have at our disposal, the treatment of this group of patients is best and most efficiently carried out with roentgen rays. As far as we can determine from comparison of the cases that we have reviewed with those reported by others, the results with roentgen irradiation are in every way equal to those with radium therapy.

Bulky, isolated, recurrent lesions should be excised if they are movable. If, on the contrary, they are fixed to the thoracic wall, or inoperable for some other reason, they may be satisfactorily treated with radium needles, or with multiple converging beams of roentgen rays. In this case, also, the lesion must be judged on its own merits and the technique of treatment individualized.

Carcinoma en cuirasse, and extensive, ulcerated, recurrent lesions are best treated with roentgen rays. In view of the gravity of the prognosis, these patients as a group should receive only mild treatment.

We have not seen a sufficient number of cases in which postoperative recurrence involved the supraclavicular lymph nodes,

to form any opinion about the best method of dealing with this lesion.

Recurrence which involves the axilla frequently is seen after incomplete radical operation. In fact, axillary recurrence is almost prima facie evidence that the original surgical procedure left some tumor in the axilla. Whatever the cause of axillary recurrence may be, such recurrence should be treated surgically if possible and the operation should be followed by intensive crossfire of the axilla as a precaution. If, on the other hand, the axillary recurrence is inoperable, we favor crossfire of the axillary space (generally through a "high voltage"* field posteriorly and one or more anterior fields at "moderate voltage,"† depending on the size of the tumor) supplemented, in selected cases, by the judicious use of buried radium. In this connection, the danger of producing an intolerable neuritis by inserting radium too near the sensory nerves must be kept in mind when planning such a combined method of treatment.

As a matter of precaution, patients who have had one recurrence of carcinoma of the breast should be examined frequently so that the disease may be kept under control. A second recurrence can, in general, be handled by the same principles of treatment as those already outlined. At this stage of the disease, it is well to modify toward the conservative side the technique planned in view of the malignancy of the tumor and the impending breakdown of the patient. Even if postoperative recurrence does not mean hopelessness, it does seem to indicate that further treatment probably will be of limited value.

RESULTS OF TREATMENT OF RECURRENT CARCINOMA OF THE BREAST

At the outset it should be stated that most of this group of patients had insufficient irradiation, as the following data will show (Table XIII). Of 25 patients treated in 1924, seventeen had one course of treatment, which often was of a mild, or even placebo, type; of the 27 patients treated in 1925, fourteen had only one course of treatment; of the 23 patients treated in 1926, four had only one course; of 35 treated in 1927, eighteen had one course; of 33 patients treated in 1928, eighteen had one course; of 33 patients treated in 1929, twenty had one course; of 27 patients treated in 1930, fourteen had one course; of 35 patients treated in 1931, fourteen had one course; of 12 patients treated in 1932, five had one course; and of 18 patients treated in 1933, twelve had one course. The reasons for this state of affairs varied, and in many instances were impossible to ascertain. In general, this group had so little treatment because of the extent and hopelessness of the recurrences.

TABLE XIII

EFFECT OF ROENTGEN TREATMENT OF RECURRENT CARCINOMA OF THE BREAST

Year	Total number cases	Less than three treatments		More than three treatments	
		Improved	Unimproved	Improved	Unimproved
1924	25		17	7	1
1925	27	1	13	10	3
1926	23		4	14	5
1927	35	2	16	15	2
1928	33		18	14	1
1929	33	1	19	9	4
1930	27		14	11	2
1931	35	2	12	17	4
1932	12		5	6	1
1933	18	1	11	3	3

As one reviews the method of treatment as it has changed from 1924 to 1934, one notices in the later years that more and more patients have been treated exclusively with roentgen rays. This change has been brought about by two factors: first, the increasing number of other lesions for which radium has been the method of choice (for example, carcinoma of the cervix) has greatly limited the facilities for treatment of these recurrent carcinomas

* High voltage = 200 kv.

† Moderate voltage = 135 kv.

of the breast with radium; second, all in all, the results of treatment with radium and roentgen rays are fairly comparable. During these years, the technique of roentgen therapy has become more and more conservative. Because the evidence for the superiority of high voltage over moderate voltage in the treatment of recurrent carcinoma of the breast seems to us to be inconclusive, and since the risk of injuring the lung with rays generated at high voltage is greater, we have adopted more and more the moderate voltage techniques as more expedient clinically. And, as far as we have been able to determine, the results of moderate voltage irradiation in the treatment of postoperative recurrence have been superior to those of high voltage treatment.

It must not be assumed, however, that all patients who have been treated with roentgen rays have been definitely benefited. Of the patients treated in 1924, one did not derive any benefit; of the patients treated in 1925, three did not derive definite improvement; and of the patients treated in 1926, five were unimproved. These all received treatment with roentgen rays of high voltage. There were two failures in 1927, one in 1928, four in 1929, two in 1930, four in 1931, one in 1932, and three in 1933. No logical or plausible reason for these failures can be offered.

The patients who were benefited can hardly be evaluated statistically. But relief of pain, cessation of hemorrhage and discharge, and decrease in the size and number of recurrent nodules in those cases in which the patients were treated exclusively by irradiation occurred with too great frequency to be only an accidental finding or coincidence. In the light of our experience, we think that at least three courses of radiotherapy should be given in order that the effectiveness of the treatment may be judged.

Looking at the results of radiotherapy in recurrent carcinoma of the breast from this point of view, one can state fairly that out of a total group of 268 patients 132 had

TABLE XIV

INCIDENCE OF METASTASIS*

Year	Other breast	Supraclavicular lymph node	Ribs	Lungs	Clavicle	Scapula	Skull	Humerus	Thoracic vertebrae	Lumbar vertebrae	Liver	Pelvis	Other (odd)
1924	2	17	2	3	0	0	0	0	0	2	1	2	
1925	1	32	7	11	0	0	2	0	1	5	4	10	
1926	1	25	2	6	0	1 (skin)	3	0	0	4	3	5	Femur 1 Cerv. 1
1927	0	31	1	7	0	1 (skin)	1	0	0	8	3	8	
1928	5	38	1	12	0	0	0	0	0	6	2	6	
1929	1	31	1	4	0	0	5	0	1	3	4	3	
1930	1	23	5	14	0	0	1	1	1	7	2	7	Skin of arm Femur
1931	1	55	4	10	1	1	2	0	3	8	4	15	Cerv. 6
1932	1	37	2	7	0	0	5	0	2	16	3	12	Tibia Embolus Parotid
1933	2	27	1	6	1	0	1	0	1	18	3	19	Cervix
Total	15	316	26	80	2	3	20	1	9	77	29	87	

* Includes all metastases.

reasonably adequate treatment. Of this group, 106 were definitely improved to some extent objectively, and 26 received no benefit or a questionable one.

METASTATIC CARCINOMA OF THE BREAST

Further evidence that the patients concerned in this review were, as a whole, in poor physical condition is given in Table XIV.

There are a few points of interest in this group which merit further discussion. Although it is impossible to prove it from the evidence available, it seems evident that the presence of metastasis to the supraclavicular lymph nodes (316 cases), the most common secondary focus found in this study, is definitely a bad sign, as it seems to precede spread of the malignant disease to the lungs and liver. In all of the 29 cases in which metastatic involvement of the liver was found, and in all but 4 of the cases in which there was metastatic involvement of the lungs, there was record of a coexistent metastasis to a supraclavicular lymph node. We could not establish any relationship between the situation of the primary carcinoma in the breast and the metastasis to the supraclavicular lymph node.

In many cases in which the liver was involved, the primary carcinoma was situated in the outer sectors of the left breast. In these cases metastasis probably took place by some route other than by direct extension through the lymphatics in the sheath of the rectus muscle.

It is also interesting to note that the incidence of metastasis to the lungs (80 cases) was about equal to the incidence of metastasis to the bones of the pelvis (87 cases). However, if one considers the total incidence of metastasis to the spinal column and pelvis (173 cases), one notices that the incidence of osseous metastasis is second in frequency only to metastasis to the supraclavicular lymph node. This should be an indication for appropriate modifications in postoperative roentgen technique.

Many patients had metastatic foci in several situations, the combination of supraclavicular with some other focus being most commonly observed. In many cases (see Table 1) there were metastatic foci without local recurrence. This was especially true in cases in which there was metastasis to the spinal column and pelvis. In this latter group of cases, the combination of metastasis to the lungs or liver with metastasis to the spinal column and pelvis was uncommon.

It is remarkable to note the low incidence of metastasis to the ribs, to the shoulder girdle, and to the other breast. A plausible explanation of this fact does not occur to us.

In many cases it was impossible to find any relationship between the grade of malignancy of the tumor in the breast and the incidence of metastasis, for in many of these cases a microscopic examination of the tumor in the breast had not been made. It seems, though, that the incidence of metastasis parallels the incidence of the various grades of malignancy, a fact which has been pointed out by Broders and Harrington. In other words, carcinoma grade 1, of the breast, is rare, and the incidence of metastasis from this tumor of the breast is low; whereas, grades 3 and 4 are the most common, the frequency of metastasis from these grades is highest, and the extent of metastasis probably is most widespread. This view is substantiated in Table XII. This table includes only cases in which the tumor was graded microscopically by Broders personally. The predominance, about 90 per cent of tumors, graded 3 and 4 may in part explain the frequency of metastasis, as well as the generally indifferent results of the treatment.

TREATMENT OF METASTATIC CARCINOMA AND OF RECURRENT AND METASTATIC CARCINOMA OF THE BREAST

For convenience, we will combine the cases in which there was metastatic carcinoma (96 cases) and cases in which both recurrent and metastatic carcinoma coexisted (87 cases) in a group of 183 cases.

From the literature which we have reviewed and our own experience, it is indefinite whether or not healing of metastasis in the supraclavicular lymph node is manifested by the disappearance of the lymph node or whether the ideal of treatment should be the control of its enlargement. For this reason, we have judged the results of irradiation of a supraclavicular lymph node, which was affected with metastatic carcinoma, from two points of view: first, whether the growth of the lymph node continued during the period of observation of the patient; and second, whether the enlarged lymph node actually became smaller. In none of the 316 cases under consideration did metastasis to the supraclavicular lymph nodes disappear completely as a result of treatment. On the other hand, in only 5 cases was there found to be a clinical note to the effect that the lymph node actually became larger than it had been before the treatment. As a matter of fact, one finds repeatedly a note that the metastasis was "controlled." We feel, therefore, that, with the information at hand, a correct evaluation of radiotherapy for this lesion cannot be made. As we have pointed out, most patients who had metastasis to the supraclavicular lymph nodes had other evidence of disease and, for the reasons previously given, were probably in the terminal stages of the malignant process.

Disregarding minor modifications, the technique by which this lesion had been handled was as follows: In the earlier years, irradiation was by means of radium packs or blocks, to the point of skin tolerance. Later, roentgen rays largely replaced radium. At present, small lymph nodes are treated by a single field of roentgen rays of moderate voltage; lesions 3 cm. or larger are treated with two anterior fields with rays generated at moderate voltage and one field posteriorly (avoiding pulmonary tissue as far as possible) with high voltage. As much as possible, the treatment is repeated at intervals of two or three months.

Metastasis to the lungs or pleura is a most unfortunate development. With carefully given roentgen treatment, we have been able, in some cases in which the patients have been in good physical condition, to lessen dyspnea from enlarged hilar nodes or to decrease the frequency of aspiration for effusion into the pleural space. We have little evidence of the beneficial effect of radiotherapy on parenchymal metastasis, except as a rare indicent.

Even less favorable is metastasis to the liver or to other abdominal organs. The response of these lesions is so indefinite and the systemic reaction from treatment so certain that, as a whole, patients with such lesions are not treated. In 29 cases in which there was metastasis to the liver, we have not seen a favorable response in a single instance. As has been indicated, the treatment of these patients was almost always of a placebo type.

Metastasis to the other breast, which occurred in 15 cases, is best treated by the principles that govern treatment of primary carcinoma of the breast; in other words, this lesion by itself is not a radiation problem. The treatment of this lesion is in general governed by the same factors (the degree of malignancy and the extent of involvement of the lymph nodes) which determine the treatment of primary carcinoma of the breast, with the reservation that prognosis is graver because of the already existing carcinoma in the other breast.

In the majority of cases (20) in which there was metastasis to the skull or brain, the patients were lost sight of too soon to enable us to form an accurate idea of the value of radiotherapy in this group. Nevertheless, relief of headache and improvement in ocular or other neurologic findings were seen often enough to prove that treatment, even of so hopeless a stage of carcinoma as this, may produce worth while palliation.

For the sake of brevity, we will consider together as one group the cases in which there was metastasis to the thoracic vertebrae (9), to the lumbar vertebrae (77)

and to the bones of the pelvis (87), a total of 173 cases. As a matter of fact, these bones were commonly involved simultaneously in a metastatic process and, as a whole, the treatment of these lesions is the same.

We[4] have previously reviewed a group of 40 cases in which there was metastatic involvement of the spinal column and pelvis from carcinoma of the breast, and have considered in detail the technique of treatment and the results to be obtained. In abstract, we may state that the lesions in the spinal column are best treated by paravertebral fields, with the beams of rays directed at the spinal column at an angle of about 45 degrees and with roentgen rays generated at 135 kv., and filtered through 6 mm. aluminum in the average case. For pelvic metastasis we favor an anterior, a posterior, and two lateral fields of roentgen rays, with the rays generated at 200 kv., and filtered through 0.75 mm. copper and 1 mm. aluminum. In each case, about 90 per cent of an erythema dose (550 r measured in air) is given to each field. With this treatment, as we have stated, about 90 per cent of patients derive improvement. It is not uncommon for recalcification of a metastatic focus to take place following treatment. Subjective and objective improvement in cases in which there is osseous involvement secondary to carcinoma of the breast is so frequent and so definite that roentgen therapy is the therapeutic method of choice for such lesions. Table XV shows the results that we have obtained in this group of cases. Improvement was obtained in more than 80 per cent of them.

Table XV

Treatment of Spinal and Pelvic Metastasis

Year	Number patients treated	Improved	Unimproved	No notes, or results indefinite
1924	4	3	0	1
1925	13	10	2	1
1926	7	5	2	0
1927	12	9	1	2
1928	4	3	1	0
1929	4	2	1	1
1930	8	6	1	1
1931	17	12	3	2
1932	19	15	1	3
1933	18	14	2	2
Total	106	78	14	14

We have not treated other miscellaneous metastases, such as metastasis to the scapula, shoulder girdle, and so forth, often enough to form any worth while opinion about the value of radiotherapy in the treatment of these lesions.

Summary

In this review the clinical aspects of a group of 573 recurrent, metastatic and inoperable carcinomas of the breast are considered.

In general, inoperable carcinoma of the breast is best treated by roentgen therapy by the technique of "multiple converging beams." In selected cases this may be combined with buried radium. Of a group of 122 patients, 42, a third of all who were treated, improved.

Recurrence of carcinoma of the breast is most commonly seen after an antecedent nonradical operation. The degree of malignancy, as judged by the method of Broders, is the most important factor in determining the probability of recurrence. Second in importance is the thoroughness of surgical operation. In the group studied, recurrence had developed in 268 cases. Operable recurrences are best treated by operation, supplemented by roentgen therapy, and the results of roentgen treatment are in every way equal to those obtained with radium. From this study, it appears that local reappearance of carcinoma in the field of operation is the most favorable form of recurrence; whereas, axillary recurrence, in general, has the worst prognosis.

One hundred and thirty-two patients out of the total number of 268 had what we regard as adequate radiotherapy. Of this number, 106 definitely improved, and

twenty-six obtained an unfavorable or uncertain result.

The most common site of metastasis in this group of cases was the supraclavicular lymph nodes, which were involved in 316 cases. The value of radiotherapy for this lesion cannot be stated for reasons given. Treatment is best carried out with roentgen rays.

Other metastatic lesions, such as involvement of the lung, or the liver, in general, respond poorly to treatment.

Metastasis to the other breast is best treated by the same method as is used in the treatment of primary carcinoma of the breast.

Osseous metastasis is the most favorable field for roentgen therapy as improvement can be obtained in more than 80 per cent of these cases.

From this review, we have little evidence for the superiority of radium or roentgen rays of 200 kv. over moderate voltage (135 kv.) roentgen rays, and, in fact, in some lesions the latter type of radiation seems superior.

It is very likely that the number of patients in this group could be greatly reduced if the frequency of a minor surgical operation as the primary treatment were reduced, and we favor radical surgical operation as the method of choice. Regardless of the method of treatment, it seems that the two important factors which determine prognosis are the index of malignancy of the tumor and the extent of metastatic involvement of the lymph nodes.*

We would like especially to express to Dr. Broders our great appreciation for his help, both for grading all the carcinomas and for his help with many of the intricate problems in the pathology of carcinoma of the breast.

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* For discussion see page 388.

THE EFFECT OF OVARIAN IRRADIATION ON THE BONE METASTASES OF CANCER OF THE BREAST*

By RICHARD DRESSER, M.D.
BOSTON, MASSACHUSETTS

CARCINOMA of the breast in young women is usually more malignant than in women who have passed the menopause; it runs a more rapid course, and ends fatally in a large percentage of cases regardless of all known therapeutic measures. Lee reviewed 191 cases of cancer of the breast occurring in women under forty years of age treated by radical mastectomy. A three year follow-up showed 15 per cent alive and free of disease. A series of 48 cases of mammary cancer in women under forty collected by the author showed only 12.5 per cent free from disease three years after radical surgical removal of the breast. Fourteen of these cases died within a year of operation.

It is generally recognized that pregnancy may cause an exacerbation of malignancy of the breast with an unusually rapid progress of the disease. An operable carcinoma is rarely observed in late pregnancy. Trout reviewed 15 cases in which pregnancy occurred after removal of a breast for carcinoma. Thirteen of these cases developed carcinoma in the remaining breast, 12 of whom died very promptly.

In 1889 Schinzinger suggested surgical removal of the ovaries in cases of cancer of the breast in young women on the assumption that the artificial menopause would retard the progress of the disease.

In 1896 Beatson, independently of Schinzinger, proposed oöphorectomy as an adjunct to the treatment of cancer of the breast in young women. He made the following observations:

1. That there seems evidence of the ovaries having control in the human body over local proliferation of epithelium. 2. That the removal of tubes and ovaries has effect on the local proliferation of epithelium which occurs in cancer of the mamma, and helps on the tendency cancer naturally has to fatty degeneration. 3. That this effect is best seen in cases of cancer in young people, a class of case where local removal of the disease is often unsatisfactory.

Beatson reported encouraging results in a number of cases treated by oöphorectomy, such as shrinkage of the primary tumor, reduction or disappearance of skin recurrences and regression of glandular metastases. There was often symptomatic relief and improvement in the general condition of the patient. Beatson had several followers among the English surgeons. Boyd collected 54 cases of which 19 showed improvement. Thomson reported 80 cases with 29 improved. Lett collected 99 cases and found improvement in about 23 per cent. If he excluded patients over fifty years of age this figure rose to 41 per cent.

Interest in this method gradually waned, but the rationale of oöphorectomy in cancer of the breast is supported by recent experimental work on ovarian hormones. Gardner et al. have observed that theelin will stimulate the mammary rudiments of the male mouse and atypical growths somewhat resembling normal and functional lobules appear in localized areas of the mammary duct system. Lacassagne (quoted by Gardner) injected male mice with a solution of folliculine benzoate. After the injection had been continued for five or six months tumors diagnosed as adenocarcinoma developed in the male mice. Goormaghtigh and Amerlinck (quoted by Gardner) studied the effect of

* The material for this publication has been collected from the Collis P. Huntington Memorial Hospital, Boston, and the Pondville Hospital at Norfolk, Mass. Read in a Symposium on Cancer of the Breast at the Twentieth Annual Meeting, American Radium Society, Atlantic City, N. J., June 10–11, 1935.

an estrogenic preparation upon the mammary glands of sexually mature female mice. Daily injections induced definite adenomatous growths in a period of a month or more.

One of the first to try roentgen irradiation of the ovaries instead of surgical castration was Foveau de Courmelles. He reported the regression of carcinoma of the breast following ovarian irradiation, and felt that the results of roentgen treatment were better and more certain than those of operative sterilization. Wintz has been using roentgen castration as a part of the treatment in cancer of the breast since 1920. He is under the impression that the method is of great importance.

Ahlbom reports the results of roentgen irradiation of the ovaries in 163 cases of cancer of the breast treated at Radiumhemmet, Stockholm, during the period 1922–1928 inclusive, 56 per cent of which had passed the menopause. Ahlbom summarizes his results as follows:

No definite proof has been forthcoming in support of the favorable effect of castration in cases of cancer at the Radiumhemmet. Yet this material includes very few of such cases in which one has the greatest reason to expect a favorable effect, if forthcoming at all, namely, menstruating women who do not give evidence of any spread of the cancer beyond the first lymphatic station. There is no evidence of the castration treatment having affected the course of the disease in any harmful way.

Hoffman has recently reported a case from the Memorial Hospital in New York which, following ovarian irradiation, showed remarkable regression of metastases from the cancer of the breast with alleviation of symptoms and improvement in the patient's general condition. Martin has reported a similar case. Roemer cites 4 cases with bone metastases from cancer of the breast which showed regression after irradiation. The ages of these women were thirty-six, thirty-nine, forty-one and forty-six respectively, all apparently in the premenopause age. Roemer implies that improvement was due to the direct effect of the roentgen rays on the metastatic lesions, but it seems more probable that the results were due to the effect on the ovaries.

Fig. 1*a*

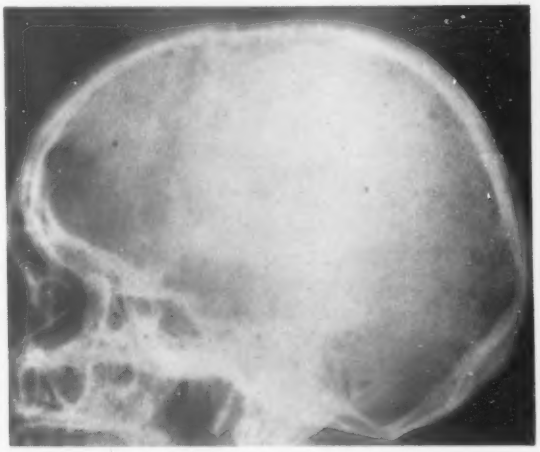

Fig. 1*b*

CASE REPORTS

In 1928 a woman aged thirty-three, was admitted to the roentgen department of the Massachusetts General Hospital. Two years previously she had noticed a lump in the right breast. A year later the breast was removed at the Huntington Memorial Hospital. The pathological report was highly malignant adenocarcinoma. At the time of her admission to the Massachusetts General Hospital she presented local skin recurrences and generalized metastases in the bones. At this time experimental work was being done on the Blair Bell

colloidal lead treatment of cancer. This patient was chosen as one of the subjects for the lead treatment. She was having rather severe pain as a result of the metastatic disease in the pelvis, and was given a moderate dose of high voltage roentgen rays over the pelvis in the hope of relieving the pain. The dosage was sufficient to cause a cessation of menstruation. Following irradiation there was definite regression of the metastatic process not only in the bones of the pelvis but elsewhere, particularly in the vault of the skull (Fig. 1, *a* and *b*). It was erroneously assumed that this regression was due to the colloidal lead treatment.

Fig. 2*a*

A year later a woman, aged forty-one, was admitted to the Pondville Hospital at Norfolk. The left breast had been amputated two years before at the Boston City Hospital. The pathological report was carcinoma. She made a good recovery from the operation and was symptom-free for about a year when she developed pain in the right lumbar region radiating down the posterior aspect of the right thigh. She went to the Peter Bent Brigham Hospital where roentgen examination showed extensive metastatic malignant disease in bones and lungs. She was given roentgen treatment without appreciable benefit and was then sent to the Pondville Hospital as a hopeless case for terminal care. Roentgen examination confirmed the observation made at the Peter Bent Brigham Hospital of extensive bone and lung metastases. There was no recurrence at the operative site. The patient was given 700 r high voltage roentgen irradiation over the lumbar spine and pelvis in the hope of alleviating the very severe pain which she suffered in this region. Her condition was so bad that it was necessary to bring her to the roentgen department on a stretcher. The radiation was sufficient to stop her menstruation. The pain was completely relieved and the patient was soon able to be up and about the ward. Follow-up roentgen examination showed most remarkable regression of the entire metastatic process in both the bones and lungs. The areas of destruction in the vault of the skull (Fig. 2, *a* and *b*) were filled in completely with new bone. There was less extensive bone regeneration in other portions of the skeleton, and pronounced diminution in the extent of the pulmonary metastases. The patient was soon able to leave the hospital and return to her usual household duties. She led an active life for three years, during which time she was largely symptom-free. She then began to develop pain in the right hip and shoulder and a little shortness of breath. Roentgen examination at this time showed that the metastatic process was again becoming active and increasing in extent. Frequent roentgen check-ups showed slow progression of the metastatic disease. In April, 1934, there was a spontaneous fracture of the femur which necessitated the patient's return to the Pondville Hospital where she died a few months later, six years after the appearance of the bone metastases.

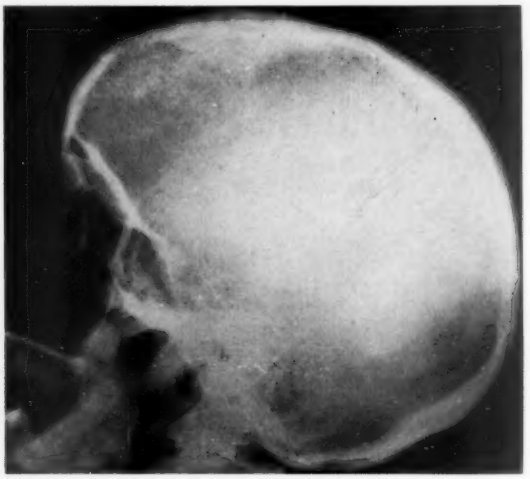

Fig. 2*b*

It has been assumed that the beneficial results obtained in these 2 cases were

entirely the result of elimination of the ovarian hormone, and on this basis ovarian irradiation has been continued in a series of cases of cancer of the breast showing metastatic disease in the bones. The following technique has been employed: 200 kv. (peak); 50 cm. distance; 0.5 mm. copper filter; 600 r, measured in air, given to the front and back of the pelvis respectively through a 15 × 15 cm. portal. This dosage is sufficient to produce permanent cessation of the menses in average-sized women thirty-five or older. In younger women and in obese individuals the depth dose should be increased, preferably by increasing the focal skin distance from 50 cm. to 80 cm. The treatment is generally given in daily doses of 300 r each. Menstruation should cease two months after the treatment is given. None of the cases has shown any untoward menopausal symptoms. It should be carefully explained to women in the child-bearing age that they will be rendered sterile, and the consent of the husband to the treatment should be obtained.

In a five year period, 1929–1934, fifty-nine cases of the cancer of the breast with bone metastases have received ovarian irradiation; 30 of these cases were women under forty-five and 29 were of post-menopause age.

Of this group of 30 who have not reached the menopause, 9 (30 per cent) have shown definite regression of bone metastases as determined by frequent roentgen examinations. The regression is manifest by destructive areas in the bone becoming hyperplastic, and in some instances a complete return to normal in the appearance of the bone. There is a concomitant relief of pain and improvement in the general condition of the patient. This improvement may continue for a period of several months to two or three years. Thirteen of this group (43.3 per cent) were temporarily relieved of pain, but showed no regression of the metastatic process by roentgen examination. In 8 cases (26.6 per cent) there was no response to treatment.

In that group which had passed the menopause not a single case showed evidence of regression of the metastatic process by roentgen examination. Fourteen of the 29 cases (48.2 per cent) experienced some relief of pain, presumably from the direct effect of irradiation to the lower spine and pelvis. Fifteen cases (51.7 per cent) were in no way benefited.

The results in these advanced cases have been so encouraging that ovarian irradiation is now being extended to a group of more favorable cases. The procedure is as follows: When a woman with cancer of the breast, who has not passed the menopause, first comes under observation, a careful local examination is made to determine the operability of the case. Soft tissue films of the breast, as recommended by Warren, have been made in many instances, but have not been found to be particularly helpful in diagnosis. Much more important is the search for distant metastases. Routine films of the chest, skull, lumbodorsal spine and pelvis are made. Metastases in the bones are slightly more frequent than those in the lungs and are often present when there is no evidence of pulmonary involvement. If metastases are found, a radical mastectomy is of course contraindicated and the case should be treated by irradiation alone. If the roentgen examination is negative and the growth is not of the inflammatory type, the breast is removed surgically. About ten days after operation high voltage roentgen therapy is given to the operative site, including the axilla and supraclavicular regions. Treatment over the ovaries is also carried out by the technique described above. The time of observation on the operable cases thus treated has been too short to draw definite conclusions, but it is the impression that ovarian irradiation will at least delay the local and metastatic recurrence of the disease.

The method is offered as a palliative measure which may be expected to be effective in about one-third of the cases treated.

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DISCUSSION OF PAPERS READ IN A SYMPOSIUM ON CANCER OF THE BREAST*

Dr. Fred W. Stewart, New York City. For diagnosis, as Dr. Adair said, we have depended on aspiration. Such evidence may be questioned by some, but we do not question its accuracy. In the greater proportion of the breasts where such diagnoses were made, persistent disease has been demonstrated after mastectomy. In others, no disease could be found remaining in the breast but the axillary nodes were positive. All stages of disappearance of tumor are to be found in the breasts.

I have a series of lantern slides which show the type of changes I have classed as the R.E.B. 3 effect. (Presented lantern slides.)

What is the chance of missing tumor in the amputated breast? On the whole, I think it is exceedingly small. If no definite area can be found we select a series of foci showing unusual arrangements of fibrous tissue, minute foci of questionable induration, etc. As to the nodes, our success in sterilizing them has been much less than in the case of the primary tumors. I think it scarcely worth while to talk about irradiation effects unless they are so profound that one cannot conceive of a reactivation of the tumor cells. If I can find in a breast or node what clearly looks like unaltered cancer nests, I call the radiation effect zero. It makes no difference to us if nine-tenths of the tumor is destroyed, provided the smaller fraction looks viable. The irradiation effects in both the breasts and the nodes are so variable within small areas that I cannot see how the effect can be other than a secondary one. One finds fully destroyed tumor and active cancer with mitoses side by side. To me this is disappointing because if the changes are largely secondary then the chances of curing these tumors by increasing doses, which are already very large from the point of view of the skin, are slight. On the whole, I am inclined to think that our results will not be greatly improved merely by increasing the doses. The time factor is, to my mind, the only logical point of next attack. Of that in all forms of glandular cancer we know essentially nothing.

What types of mammary cancer disappear under the methods employed? We cannot say. Aspiration biopsies do not tell us anatomical or histological types. When the treatment is really successful the tumors have gone so far toward total disappearance that one cannot tell what

* Papers of Auchincloss, Meland, Adair, Leddy and Desjardins, and Dresser.

their types were. However, we can say that all histological varieties have persisted after this treatment and hence it is likely that we may conclude that no one type is peculiarly sensitive. That again makes me believe that we are dealing largely with secondary effects.

DR. DALLAS B. PHEMISTER Chicago. Dr. Auchincloss has outlined the therapeutic procedure which in general I have followed for cases of carcinoma of the breast. If operable the case is treated by radical amputation followed by roentgen irradiation. Dr. Auchincloss has shown the numerous routes by which carcinoma may spread through the lymphatics. I wish to call attention to lymphatic spread to the opposite breast, which is not uncommon, the metastasis developing most frequently beneath the nipple. Postoperative irradiation of the opposite breast has not always received the attention which it warrants. As to the bone metastases, I believe that they arise by spread of the carcinoma through the lymphatics to the blood stream with eventual lodgment and growth in the bones. Of course, the lungs, muscles, and other tissues receive carcinoma cells from the blood stream, but they do not grow in these locations, and particularly in the muscles as frequently as in the bone. The reason for this is unknown. After excision of carcinoma by radical operation, undetected metastases are often left behind. These often fail to grow or grow extremely slowly for many years. This was brought out by Leddy's statistics showing that the majority of recurrences were in patients who had been operated on five years or more previously. It appears that the body exercises a carcino-static effect on small metastases after removal of nearly all of the tumor. Dr. Adair's favorable results because of preoperative irradiation are substantiated by the experience of the medical profession in Sweden.

DR. ROBERT B. GREENOUGH, Boston. There are two points I wish to mention. First I would like to encourage our Chairman, Dr. Grier, a little in regard to the value of public education in the cancer problem. In Massachusetts we have had excellent cooperation between the cancer committee of the State Medical Society, the State Department of Public Health and the Massachusetts branch of the American Society for the Control of Cancer. They have united in making concerted efforts to educate the people of Massachusetts. The Public Health Department has directed its efforts toward lay education, and that of the medical profession has been carried on through the Cancer Committee of the State Medical Society. As a result of this work we feel that there has been improvement and that cancer is discovered earlier than it used to be. This is shown by the fact that the duration on admission to the hospital of the various types of cancer has been steadily diminishing year by year. Whereas in 1914 only 20 per cent of the operable cases of breast cancer came in without axillary involvement, in 1927, 40 per cent of these cases were in this early favorable group. That means we are getting cancer of the breast earlier, and I think this applies to cancer of other organs also. I think this is a very important feature of the whole cancer problem. I would even go so far as to say that an increase of 5 to 10 per cent in the proportion of cases of cancer that are discovered while still at their point of origin counts for more than any improvement in surgery or any addition to our resources for treatment that has been introduced in many years.

Another point I wish to make is that I feel that our approach to irradiation in cancer of the breast, either preoperative or postoperative, has been on a somewhat mistaken basis. This is a rather strong statement but what I wish to bring out is that surgical treatment of cancer of the breast, when properly carried out, which it is not always, is capable of getting rid of the *local* disease in approximately 80 per cent of the operable cases, although perhaps only 35 per cent remain free of the disease at the end of the five year period. The difference between the 80 per cent and the 35 per cent is made up of the group who die from metastases in the lungs, bones, supraclavicular glands, or other organs which were not discovered at the time of operation. In cases with metastasis to the spine the lesion may exist for as long as six months and cause symptoms before definite roentgen evidence of the lesion can be obtained. We know it must take some little time for a group of cells in the deeper part of the body to grow large enough to make themselves evident. The trouble is that in the beginning we cannot determine the exact extent of metastatic disease. In the case of involvement of the axillary glands we found discrepancy between the clinical and the microscopic evidence of metastasis. On microscopic examination 33 per cent showed cancer when it was not evident

clinically. In the cases thought clinically to be involved, the gland was enlarged, not by reason of cancer but for some other reason, in some 22 per cent of the cases. As long as our clinical estimate of the extent of disease is as crude as this we must admit that examination for deep metastases must show an even greater percentage of error.

I think therefore that the attention of radiologists should be directed not so much to the locality of the disease that is to be operated upon as to other regions where metastatic disease may be present but can be definitely demonstrated only with the greatest difficulty, if at all, in the earliest stage of its development.

Dr. Henry Schmitz, Chicago. I have been particularly interested in the last paper by Dr. Dresser on the production of castration by radiation therapy in cancer of the breast. The treatment rests undoubtedly on physiologic observations. In 1922 Rosenburg published microscopic investigations of breasts removed post mortem from women in whom the exact date of the last menstruation was known. He found that the epithelium of the breast and the glands show hyperplasia as seen in the budding and branching. He thought the condition to resemble the premenstrual hyperplasia of the endometrium in the menstruating woman.

Just as we may have a persistent hyperplasia in the endometrium, so it is evident that we may have persistent hyperplasia of the epithelial cells and glands of the breast. Disturbances occur with disturbances in function of the corpus luteum due to a disturbance in the anterior pituitary gland or the pineal gland. Recently a paper was published by Geschickter et al., on breast hyperplasias. The observation was that in some cases prolan was obtained from the tissues. The use of prolactin caused complete resolution of the hyperplastic tissues in gynecomastia, but failed to obtain similar results in the female. Prolactin is not formed in the pituitary in the presence of functioning corpora lutea. Had the latter been suppressed, prolactin would probably have caused resolution of hyperplasia in the female. Recently an investigator published investigations on pineal gland extract. He has found that the hormone arrests the activity of the corpus luteum. Should this observation be corroborated by other investigators then a solution for the prevention of hyperplasias of the breasts would be found.

It seems reasonable to conclude that under the influence of the corpus luteum in menstruating women, breast carcinomas are greatly stimulated by corpus luteum hormone. Radiation castration suppresses the hormone entirely and thus assists in the palliative effects reported by Dr. Dresser.

Dr. Maurice Lenz, New York City. I would like to emphasize one point, stressed by the late Dr. Lee, namely, that in evaluating surgical or irradiation treatment of cancer of the breast, the natural course of the disease should be taken into account.

The patient, whose lantern slide I am demonstrating, had an untreated carcinoma of the left breast which gradually eroded the entire breast by ulceration, during the twenty-two years preceding the time I treated her for generalized metastases. Had she been operated on or treated by irradiation in the early part of her tumor history, one could have claimed for the treatment several five year survival periods.

With reference to our ability to permanently arrest cancer of the breast by external irradiation, I would like to call your attention to our experiences at the Presbyterian Hospital, New York City. We exposed 8 cases to 3,000 r (without back-scattering) at 200 kv., and two months later did a mastectomy. In each of those 8 cases the pathologist was able to discover cancer cells. This makes it appear doubtful whether we may hope to frequently permanently arrest, with smaller dosage, hidden foci of cancer cells in the mediastinal, supraclavicular or paravertebral regions. These, however, are the very areas, as Dr. Greenough pointed out, in which the surgeons expect our help. The primary tumor of the breast they hope to remove entirely, and theoretically, at least, this site should not require any irradiation. From a practical standpoint the thin, poorly nourished skin flap after a thorough radical mastectomy cannot stand 3,000 r. Growth restraint of cancer of the breast can undoubtedly be accomplished with smaller roentgen dosage in a number of cases.

Dr. Auchincloss (closing). I am very much interested in the effect of radiation on inoperable lesions. So-called operable cases may have axillary metastases. At the Memorial Hospital axillary metastases do not disappear with irradiation. Our experience is that after a thorough radical operation local metastases do not appear in the axillary and subclavian regions,

nor in the skin flaps, except in far advanced cases. They occur beyond the operative field, in the chest wall and outside the operated area. Why submit "operable cases" to irradiation when it is demonstrated that it does not cause the disease to disappear and the very same tissues can be made to disappear if carefully removed by operation? Such experimental work scarcely seems justified at the present time.

Dr. Meland (closing). I am glad the point that these growths are very resistant to radiation has been emphasized. We are not getting very far if we cannot control the primary lesion, for the patient always dies of the extension of the disease, not the primary lesion.

Another factor was brought out in the paper by Dr. Dresser. Dr. Ullmann informed me that they are doing some work at the Cottage Hospital in Santa Barbara with the pituitary gland in tumor-bearing animals. They have been irradiating these animals very thoroughly over the pituitary and have found in quite a large percentage that primary tumors have regressed without any further treatment.

Dr. Adair (closing). The literature and all the groups of men who have ever discussed preoperative irradiation have always brought out the point that breast carcinoma is very resistant to irradiation. I think that is a fair statement. On the other hand, radiation therapy is a very young science in comparison with other branches of medicine and I think we must have a very open mind, and a very cooperative mind, and not condemn too hastily. I think that is the trouble. In surgery, after all, we are only accomplishing, as a rule, cure in about one out of three cases of operable breast carcinoma. I think we must work out some way in which gradual improvement can be brought about, and I believe in the last few years radiation therapy has accomplished a great deal. Of course, it has a long way to go but I think five years from now ulceration of the breast following irradiation will be very rare in medical annals.

I was much interested in Dr. Dresser's paper and consider it a very constructive bit of information. I wish to know his idea of why the pain disappeared in these patients who had only irradiation of the ovaries.

Dr. Dresser (closing). Answering Dr. Adair's question as to why pain disappears after irradiation, I do not know, but this occurs in about 50 per cent of the cases. This may happen even though there is no visible regression of the metastatic process. We found that out a good many years ago when high voltage roentgen therapy was quite new and we were treating many cases of carcinoma of the prostate from the Brady Clinic. I do not recall any case in which regression of the metastases occurred, but there was remarkable relief from pain. This whole subject of endocrinology and its relation to carcinoma offers a very fertile field for investigation.

THE EFFECT OF RADIUM IRRADIATION ON THE ELECTROPHORETIC VELOCITY, VIABILITY AND pH OF *ESCHERICHIA COLI* SUSPENSIONS*

By K. PIERRE DOZOIS, M.S., GRANT E. WARD, M.D., F.A.C.S., *and* FRANK WILSON HACHTEL, M.D.
BALTIMORE, MARYLAND

THE electrophoretic migration of a bacterial cell may be defined as the movement of the cell through the dispersion medium, due to an imposed E.M.F. Those effects which disturb the orientation of the electrically organized interface causing a change in the zeta potential are effects on the Helmholtz double layer of the bacterium.

Bacteria, under normal conditions, carry a negative electrophoretic potential. A viable bacterium has a definite electrophoretic migration velocity and as viability decreases the velocity also decreases until it reaches a minimum. The light waves of bactericidal nature reduce the zeta potential of the organism: the more penetrating and the greater the absorption of the waves, the greater will be this decrease. The extent of this reduction may be determined by measuring the electrophoretic potential with a microcataphoresis cell (Jordan and Falk;[8] Ellis and Wells;[5] Clark;[3] Winslow, Falk and Caulfield;[17] Falk et al;[6] Shaughnessy and Criswell;[14] Abramson and Muller[1]).

The effect of ultraviolet radiation on the electrophoretic migration velocity of *Escherichia coli* has been reported by Lisse and Tittsler.[10] Dozois, Tittsler, Lisse and Davey[4] studied "The effect of low voltage x-rays on the electrophoretic migration velocity viability and pH of Escherichia coli suspensions." The fact that ultraviolet radiation influences the electrophoretic migration velocity while low voltage roentgen rays do not has led to the studies of the effect of radium irradiations.

Warren (1928) has demonstrated that bactericidal rays must be those that are absorbed by the materials acted upon. Henri[7] has shown that those rays which have the greatest bactericidal power are absorbed by proteins. It is also known that the rays absorbed have a very specific range, and that wave lengths either longer or shorter are less active. Although Bovie[2] has shown that Schumann rays (1,230 to 1,850 Å) are more reactive than the longer waves, it appears that rays within the range of the ultraviolet light are the most effective.

The purpose of this study was to determine whether the short waves of radium are absorbed, and, if so, whether they have a bactericidal effect, and influence the electrophoretic migration velocity.

TECHNIQUE

Preparation of the Suspension. Three strains of *Esch. coli*, which have given consistent readings of the electrophoretic migration velocity during previous studies of a similar nature, were used in investigating the effects of radium irradiation. These cultures were grown on proteose-peptone agar slants of an approximate pH of 6.8 for twenty-four hours at 37°C. The zeta potential varied until the cultures were eighteen hours old and then remained constant for forty-eight hours. These observations verify to some extent those of Shibley,[15] who has shown that the zeta potential varies until the cultures are about eighteen hours old, after which it remains constant. The growth on agar was removed by washing the surface with a small quantity of distilled water. The suspension was filtered through cotton and centrifugalized at about 2,700 r.p.m. for forty-five minutes. The supernatant fluid was removed, the cells resuspended in distilled water and rewashed three times, as advocated by Northrop and de Kruif.[11] After the last washing the cells were filtered through filter paper and collected in a clean flask and standardized. All glass-

* From the Department of Bacteriology and the Department of Oncology of the University of Maryland Medical School, Baltimore.

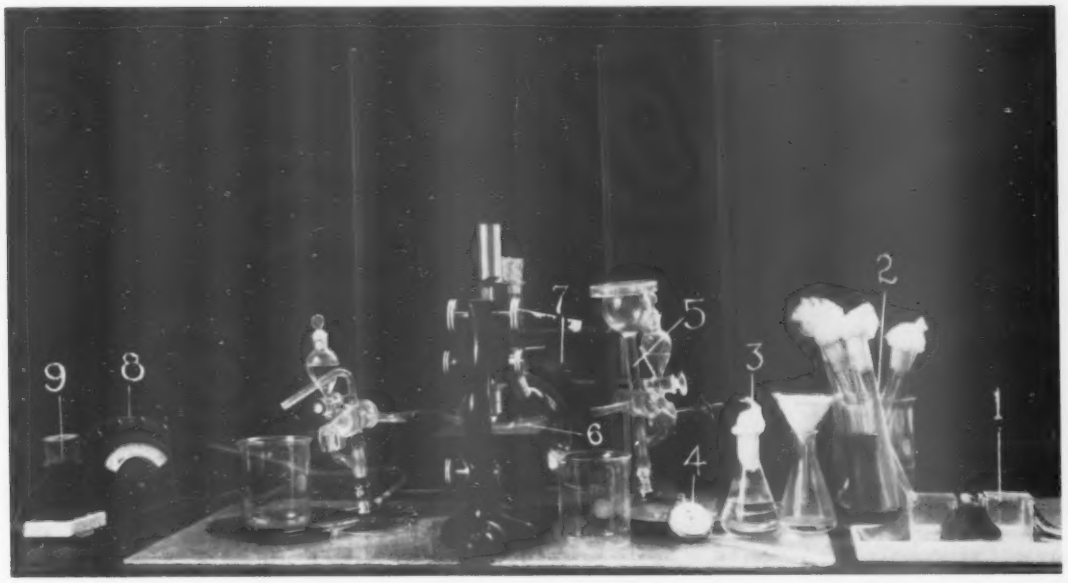

Fig. 1. Complete apparatus used. 1. Irradiation dish. 2. Cultures. 3. Bacterial suspension for irradiation. 4. Stop watch. 5. Electrophoretic apparatus. 6. Microcataphoresis cell. 7. Micro lamp. 8. Weston voltmeter. 9. Switch to control current.

ware was chemically cleaned with cleaning solution and distilled water. About 200 c.c. of each suspension, of a pH 6.8, was prepared. Twenty-five cubic centimeters were placed in each of four glass cells, two for irradiation and two to be used as controls. It was not necessary for the irradiated suspension to be further diluted. Readings were made immediately following irradiation and at other intervals as indicated.

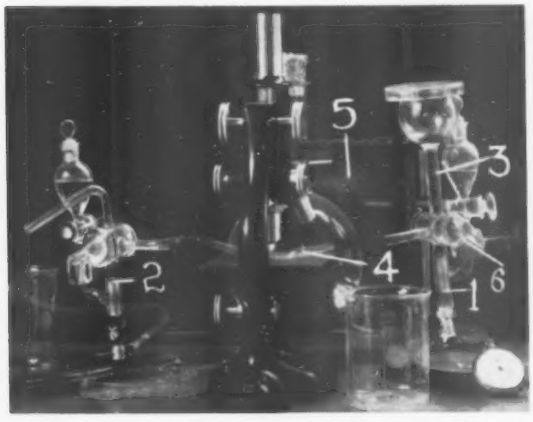

Fig. 2. The Kunitz modification of the Northrop-Kunitz microcataphoresis cell. 1, 2. Zinc electrodes. 3. Bacterial suspension ready to flow into cell. 4. Microcataphoresis cell. 5. Micro lamp. 6. Stopcock to control suspension flow.

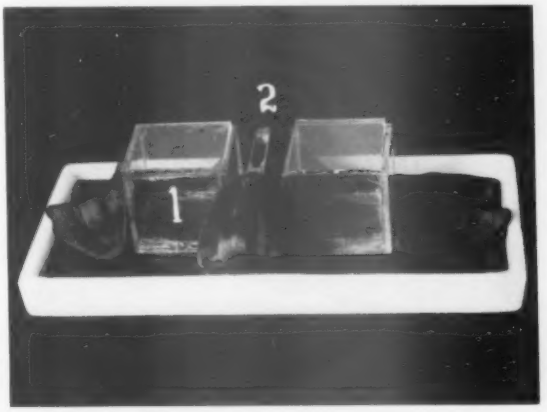

Fig. 3. Irradiation dish. 1. Glass cell to hold suspensions during irradiation. 2. Container to hold radium during irradiation.

Viability was determined by ordinary plate counts and the pH studies were made by colorimetric measurements (W. A. Taylor slide comparator) on both the irradiated and control suspensions.

RADIUM APPARATUS AND TECHNIQUE

Four water-tight cells 1½ inches square, inside dimensions, which could be taken apart and washed, were made by cementing together lead-and-aluminum-free glass plates. A rubber tray was made into which two glass cells and the radium-containing aluminum dish could be

placed and held in position during the irradiation. The cells were so placed that the centers of the radium tubes were one-half inch from one inner surface of each cell, and thus one-half inch from the surface of the liquid and 1¼ inches from the center of the liquid. The suspensions in each cell received equal amounts of radiation. During the irradiation the apparatus was placed in a dark ice box at a temperature of 5°C. The control cells were also kept in the ice box but at least 4 feet away from the radium-containing tubes—a distance sufficient to avoid being affected by the radium.

MEASUREMENTS OF THE ELECTROPHORETIC MIGRATION VELOCITY

The Kunitz[9] modification of the Northrop-Kunitz microcataphoresis cell was used with a micro lamp and a Bausch and Lomb 8 mm., 0.50 n. a. 21x objective, and 10x eyepiece. After the microcataphoresis cell had been filled with the suspension the current was applied for six minutes before a reading was made. This was sufficient time for the bacteria to reach a maximum velocity. Only those cells in sharp focus were measured. Twenty readings were made at two stationary levels, i.e., 0.21 and 0.79 of the inside depth of the cell. An applied potential of 118 volts was used. This voltage gave a potential drop through the cell of 2.5 volts. The results are expressed in terms of 0.5 mm. per second at 118 volts.

Radium Filtration

Amount of radium element used—70 milligrams.
Radium tubes of 1 mm. wall of platinum and gold.
Aluminum box wall 1 mm. thick.
Glass wall of cell 3 mm. thick.
Distance from surface of suspension—½ inch (1.25 cm.).
Distance from center of liquid suspension—1¼ inches (3.1 cm.).

Although it is difficult to state the exact wave length employed in these experiments, it is usually accepted that the beam coming through 1 mm. of platinum is made up largely of wave lengths varying from 0.06 Å down to approximately 0.002 Å. There is, however, evidence that there are some wave lengths greater than 0.06 Å and some less than 0.002 A. The bulk of the secondary rays from the platinum are absorbed by the aluminum. The chief aim in this set-up was to use a beam similar to that employed in our therapeutic applications.

As an erythema dose we give 250 to 300 mg-hr. per 1½ square inches, at ¼ inch distance from the skin, filtered through 1 mm. of platinum and aluminum foil, the distance being maintained by wax or felt. This amount of radiation causes an erythematous blush and slight desquamation in infants treated for hemangiomata, a rather delicate test. At ½ inch distance, that is, the distance from the center of the radium tubes to the surface of the liquid suspension of bacteria, the erythema dose would be approximately 700 to 800 mg-hr., a dose slightly below that delivered in experiment 12 (Table I, A, B, and C). Of course the total irradiation of the suspension was far below this, as the preparation was 1½ inches square. Thus the bacteria on the far side receive less than those on the proximal side.

The average mean distance from the radium to the suspension is 1¼ inches, that is, from the center of the radium tubes to the center of the liquid. At such a distance the erythema dose would be approximately 1,600 mg-hr., a little more than that given in Experiment 21 (Table I, A, B, and C).

TABLE I, A

ELECTROPHORETIC MIGRATION VELOCITIES OF REPEATED EXPERIMENTS SHOWING THE EFFECT OF AGE AND RADIUM IRRADIATION

CULTURE 27F.

Age in hours	Velocity 0.5 mm. in sec. (Control)	Radium doses in mg-hr.	Velocity after irradiation 100 u. per sec.	Percentage deviation from normal
Control	15.33		15.4	0.46
1	15.46	70	15.25	−1.36
2	15.33	140	15.62	1.89
3	15.26	210	15.8	3.54
4	15.43	280	16.6	7.58
5	15.46	350	17.1	10.61
6	15.40	420	17.9	16.23
7	15.40	490	18.75	21.28
12	15.46	840	19.6	27.03
14	15.43	980	20.2	32.89
16	15.20	1,120	20.8	35.68
18	15.33	1,260	21.3	39.22
21	15.4	1,470	21.6	40.26
28	15.4	1,960	22.0	42.86
35	15.46	2,450	23.0	49.42
42	15.30	2,940	24.2	58.17

TABLE I, B

CULTURE 27F.

Age in hours	Velocity 0.5 mm. in sec. (Control)	Radium doses in mg-hr.	Velocity after irradiation 100 u. per sec.	Percentage deviation from normal
Control	15.26		15.6	2.23
1	14.93	70	15.55	4.15
2	15.23	140	15.55	2.10
3	15.33	210	16.1	5.02
4	15.34	280	16.50	8.37
5	15.26	350	16.63	8.98
6	15.06	420	17.00	12.88
7	15.23	490	17.40	14.25
12	15.26	840	18.30	19.92
14	15.23	980	19.42	27.51
16	15.26	1,120	20.3	33.03
18	15.4	1,260	21.52	39.74
21	15.33	1,470	22.0	43.51
28	15.3	1,960	23.4	52.94
35	15.4	2,450	23.92	55.32

TABLE I, C

CULTURE 2031

Age in hours	Velocity 0.5 mm. in sec. (Control)	Radium doses in mg-hr.	Velocity after irradiation 100 u. per sec.	Percentage deviation from normal
Control				
1	13.9	70	.38	−0.72
2	14.1	140	14.3	1.42
3	13.8	210	14.4	4.35
4	14.2	280		
5	14.0	350	15.3	9.29
6	14.2	420	15.6	9.86
7	13.8	490	15.7	13.77
9	14.3	630		
12	14.1	840	16.6	17.73
14	14.3	980	18.25	27.62
21	14.4	1,470	19.00	31.94
28	14.4	1,960	21.5	49.31
35	14.2	2,450	22.4	57.75

EXPERIMENTAL RESULTS

The results of the measurements of the electrophoretic migration velocities (Table I, A, B, and C) show that the gamma rays of from 0.06 to 0.002 Å do influence the zeta potential of the bacteria. As the dose increases the zeta potential decreases, and the length of time, in seconds, which it takes the bacteria to travel over the unit distance (0.5 mm.) under a unit of applied E.M.F. (118 volts) increases. The percentage of decrease in the zeta potential remains fairly constant for the three strains of *Esch. coli* studied, and the maximum percentage of decrease in the zeta potential is reached with a dosage of 2,940 mg-hr., or approximately 1.84 erythema doses.

Each reading in Table I, A, B, C is the average obtained from three different experiments carried on over a period of time, conditions being duplicated as near as possible each time.

TABLE II

RESULTS OF VIABILITY STUDIES

Radiation doses mg-hr.	No. of viable cells per cubic centimeter		Percentage decrease
	Control	Irradiated	
3			
210	1,950,000	1,880,000	− 3.58
7			
490	2,310,000	1,880,000	−18.13
12			
840	2,500,000	1,940,000	−22.40
14			
980	2,120,000	1,480,000	−30.19
18			
1,260	1,980,000	1,310,000	−33.84
21			
1,470	2,100,000	1,300,000	−38.09
28			
1,960	1,920,000	970,000	−50.00

In Table II each figure recorded is the average result of three plate counts. The number of viable cells per cubic centimeter decreases as the dosage increases, and the percentage of decrease reaches a maximum with a dosage of 1,960 mg-hr. or 1.22 erythema doses. These doses were not carried so high as in the experiments to determine the effect upon electrophoretic migration velocities, but it is reasonable to suppose the results would have been similar.

The results of the pH determinations (Table III) show that radium, in the doses

TABLE III
RESULTS OF pH DETERMINATIONS

Irradiation dose mg-hr.	pH	Suspensions	
	Distilled Water	Control	Irradiated
3 210	6.6	6.8	6.8
7 490	6.6	6.7	6.8
12 840	6.6	6.8	6.8
14 980	6.6	6.8	6.7
18 1,260	6.6	6.6	6.6
21 1,470	6.6	6.8	6.8
27 1,890	6.6	6.8	6.8

studied, does not alter the pH of the suspensions of *Esch. coli*.

DISCUSSION

The results in Table I, A,B,C, which show that the gamma rays of from 0.06 to 0.002 Å do influence the zeta potential of the bacteria is not in accord with the findings of Dorn, Baumann and Valentiner (1905). These workers have shown that the lethal action of radium is attributable to the alpha and beta particles, and that the gamma rays are apparently harmless.

Comparing Experiment 21 (Table I, A,B,C) with Experiment 21 (Table II), we find that 1,470 mg-hr. irradiation—a little under the calculated erythema dose of 1,600 mg-hr.—decreases the viability of the bacteria in the preparation by 38.09 per cent. Zinsser and Bayne-Jones[18] show that there is conflicting evidence in the literature on the effect of radium upon bacteria, but that workers have found that radium emanations kill *Esch. coli*, *Staph. aureus* and other pathogenic bacteria after long exposures. Theoretically then, such irradiation should have a beneficial effect upon infections, for example, carbuncles. Such is actually the case, and radium packs do greatly benefit carbuncles and subcutaneous abscesses.

It is generally accepted that slightly less than an erythema dose of roentgen rays, properly filtered, will act in like manner, so that roentgen therapy is rapidly becoming the treatment of choice for carbuncles. Some unknown biophysical phenomenon must come into play during such irradiation of infections, however, for low voltage roentgen rays do not have the same bactericidal action on suspensions (Dozois, Tittsler, Lisse and Davey[4]) as do the gamma rays of radium. Further investigation is necessary to understand more thoroughly the results obtained by irradiation of infections.

Ultraviolet rays, on the other hand, which are much longer waves than gamma rays of radium or roentgen rays, have the greatest bactericidal action of the three, but so far as is known are not used for the treatment of carbuncles. This may be because of their limited penetration, as some more superficial infections are benefited by ultraviolet radiation.

In this connection it is interesting to mention that waves much longer than any of the above have been used in the treatment of superficial and deep infections. Schliephake[12] has studied the effect of radio waves ("ultrashort waves") from 3 to 18 meters long. Heat effects are observed with these waves and it has not been possible, as yet, to determine to what degree wave length is responsible for the beneficial therapeutic results. Schliephake says that wave length is not a very important factor in treating superficial infections, such as furuncles and carbuncles, but that in the deeper ones, better results are obtained with the shorter waves. This might be explained by the fact that the shorter waves are more penetrating, but there is a possibility of specificity of action of the band of waves employed.

The results of the pH determinations (Table III) show that radium, in the doses studied, does not alter the pH of the suspension of *Esch. coli*. The effects of cations upon bacterial viability have been studied by Winslow and Dolloff.[16] Since the hydro-

gen ion concentration may have an effect on the bacterial viability, it was important to note whether an alteration in the pH of the bacterial suspension produced the change in viability or whether it was due to the radium irradiation. Since there was no change in the pH this did not play a part. Lisse and Tittsler[10] have found an increase in the pH of suspensions after lethal doses of ultraviolet radiation, while Dozois, Tittsler, Lisse and Davey[4] have demonstrated that roentgen rays, of the wave lengths studied, did not alter the pH.

SUMMARY

1. The electrophoretic migration velocity of suspensions of *Escherichia coli* is reduced by irradiation with gamma rays of radium. As the dosage increases the velocity decreases.

2. Radium irradiation does influence the viability of the bacteria studied.

3. The percentage of decrease in the electrophoretic migration velocity corresponds to the decrease in viability.

4. Radium irradiation has little or no influence on the pH of the suspension.

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Twenty-first Annual Meeting: Kansas City, Mo., May 11–12, 1936.

EDITORIAL

ROENTGEN THERAPY OF ACUTE INFLAMMATIONS AND INFECTIONS

A QUESTION which has been recurring frequently in the minds of some during the last few years is this: Does the medical profession in general and the roentgenologist in particular realize and appreciate the remarkable value of roentgen therapy in the treatment of acute inflammations and infections, almost regardless of the cause, nature, location or extent? I am inclined to believe that they do not, because little note is made of this treatment in even the most recent textbooks, and only infrequent and limited evidence of it is to be found in the index of the medical literature of this country. On the other hand, the roentgen literature of Europe, especially of France, Germany and Austria contains many references to its use and value.

In this country, Hodges[1] of Richmond has been a most enthusiastic advocate of roentgen therapy of infections and has published a number of articles on this subject. The most recent appeared in this Journal for February, 1936, and is a comprehensive review of the various infections in which roentgen therapy has been found of value. He also deplores the fact that the value of irradiation in infections is not more universally realized.

Some means should be found to extend the use of roentgen radiation in this group because there is no therapeutic measure in the whole practice of medicine more positive or beneficial in any disease. One might by way of analogy compare its effect to that of quinine in malaria. Quinine was used many years before its specific effect was known. The specific effect of roentgen radiation on infections may not yet be understood, but, empirically, under proper use and favorable circumstances, it is just as valuable as quinine was before the malarial parasite was discovered.

The rules as to how much and when to give the radiation are simple. The dose in roentgens must always be small, not more than 100 r being administered. The best time to give the radiation is the earliest possible moment after there is evidence of inflammation or infection. Frequently only one treatment is necessary, but these small doses may be repeated at intervals of two or three days. When treated early enough, the vast majority of pyogenic infections do not even suppurate. This is strikingly true of carbuncle, furuncle, felon, and infections following pin or needle punctures. There is one exception, that is in the case of carbuncles. Patients with high blood sugar are not greatly benefited. Even if suppuration has taken place, there is much to be gained, because the inflammatory area promptly becomes smaller, drainage is more free, and the course is materially shortened. Pain sometimes becomes more severe for a few hours after treatment, but then becomes less and usually disappears rather promptly.

Roentgen therapy does not and should not interfere with any of the other recognized methods of treatment, except that poulticing should rarely be done. It is not necessary and may cause suppuration where it would not occur otherwise. When pus is present, it must be drained surgically.

This form of treatment is not advocated in those conditions in which there is a

[1] Hodges, Fred M. Roentgen therapy of certain infections. Am. J. Roentgenol. & Rad. Therapy, February, 1936, *35*, 145–155.

specific antidote, such as in diphtheria, tetanus, and so forth. However, it is worthy of note, and probably largely forgotten, that Hickey in 1922 proved that a high percentage of diphtheria carriers could be rid of the bacilli by roentgen therapy; this is true also of typhoid carriers.

In the way of remedying the lack of knowledge of the value of irradiation in infections, one method would be for all roentgenologists, especially those in charge of large hospitals, to go to the chief of every department in the hospital and ask to be permitted to treat every patient who has an active infection. The dispensary, as well as the ward patient, should be included. Patients who cannot or should not be moved to the roentgen department, as, for example, those having a contagious infection such as erysipelas, may be treated in their beds with portable apparatus; but such equipment should be calibrated just as carefully as the more powerful apparatus, because, no matter where given, the dose must be not more than 100 r. In superficial lesions, the question of voltage, filtration, and distance are of little importance. Deep lesions, such as pelvic infections, should, however, be treated with moderately high voltage, and filtration of from 4 mm. aluminum to 0.5 mm. copper. Judgment and skill in this treatment are required just the same as in the use of morphine for pain. No harm can come of it if not carried too far; on the other hand, so much good will be gained that the surgeon and the internist, as well as the patient, will be grateful.

There is one more important consideration. The roentgenologist should make a photograph of each patient, both before treatment, and later, to show the result. Then at future meetings of the American Medical Association, and other medical meetings, convincing exhibits could be arranged to show the medical profession, as a whole, the value of the treatment.

Willis F. Manges

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. E. P. Pendergrass, University Hospital, Philadelphia, Pa. Annual Meeting: Cleveland, Ohio, Sept. 29–Oct. 2, 1936.

American College of Radiology
Secretary, Dr. B. H. Orndoff, 2561 N. Clark Street, Chicago, Ill. Annual meeting: Kansas City, Mo., 1936.

Section on Radiology, American Medical Association
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: Kansas City, Mo., May 11–15, 1936.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N.Y. Annual meeting, 1936: To be announced.

Radiological Section, Baltimore City Medical Society
Secretary, Dr. W. B. Firor, 1100 N. Charles St., Baltimore. Meets third Tuesday each month, September to May.

Radiological Section, Connecticut State Medical Society
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets annually in May. Special meetings may be called by the Chairman.

Radiological Section, Los Angeles County Medical Society
Secretary, E. N. Liljedahl, Los Angeles, Calif. Meets on the second Wednesday of each month at the County Society Building.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas. Annual meeting, Baltimore, Md., Nov. 17–20, 1936.

Brooklyn Roentgen Ray Society
Secretary, Dr. E. Mendelson, 120 E. 19th St., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

Buffalo Radiological Society
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

Chicago Roentgen Society
Secretary, Dr. R. G. Willy, 1138 N. Leavitt. Meets second Thursday of each month October to May inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. H. G. Reineke, General Hospital Cincinnati, Ohio. Meets third Monday of each month, October to May, inclusive.

Cleveland Radiological Society
Secretary, North W. Shetter, M.D., 14600 Detroit Ave. Meetings are held at 6:30 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

Denver Radiological Club
Secretary, Dr. K. D. A. Allen, 452 Metropolitan Building, Denver, Colorado. Meets on any month having a fifth Monday.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne Country Medical Society Building.

Florida State Radiological Society
Secretary, Dr. Gerard Raap, Miami, Florida. Meetings held twice a year, May and November.

Illinois Radiological Society
Secretary, Dr. Cesare Gianturco, 602 W. University Ave., Urbana, Ill. Regular meetings held quarterly.

Indiana Roentgen Society
Secretary, Dr. J. N. Collins, Indianapolis, Ind. Meeting held the second Sunday in May annually.

Long Island Radiological Society
Secretary, Dr. M. Dannenberg, 1464 Eastern Parkway, Brooklyn, N. Y. Meets on third Thursday of each month from October to May, at 8:30 P.M.

Michigan Association of Roentgenologists
Secretary, Dr. C. S. Davenport, St. Lawrence Hospital, Lansing, Mich. Three meetings a year, Fall, Winter, and Spring.

Milwaukee Roentgen Ray Society
Secretary, Dr. S. A. Morton, Columbia Hospital, Milwaukee, Wis. Meets monthly. Place of meeting designed by the president.

Minnesota Radiological Society
Secretary, Dr. L. G. Rigler, University Hospital, Minneapolis, Minn. Meets in St. Paul, Minn., in March, 1936.

Nebraska State Radiological Society
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday evening of each month.

New England Roentgen Ray Society
Secretary, Dr. Thomas R. Healy, 370 Marlboro St., Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

Radiological Society of New Jersey
Secretary, Dr. P. S. Avery, New Brunswick, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by the president.

New York Roentgen Society
Secretary, Dr. E. F. Merrill, 30 W. 59th St., New York. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

North Carolina Roentgen Ray Society
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

Central New York Roentgen Ray Society
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse, N. Y. Three meetings a year—January, May, and November.

Pacific Roentgen Club
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. L. E. Wurster, Williamsport, Pa. Next annual meeting June 5 and 6, 1936, Lycoming Hotel, Williamsport, Pa.

Philadelphia Roentgen Ray Society
Secretary, Dr. Thomas Loughery, Germantown Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. W. W. Fray, Strong Memorial Hospital. Meets monthly on second Thursday from October to May, inclusive, at 7:45 at the Rochester Medical Association Building.

St. Louis Roentgen Ray Society
Secretary, Dr. P. C. Schnoebelen, Missouri Bldg., St. Louis, Mo. Meets first week of each month. Time and place of meetings designated by president.

South Carolina X-Ray Society
Secretary, Dr. R. B. Taft, 105 Rutledge Ave., Charleston Meets at time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary-Treasurer, Dr. J. H. Smith, Lubbock, Texas.
Meets annually one day preceding the meeting of the Texas State Medical Association.

University of Michigan Department of Roentgenology Staff Meeting
Secretary, Dr. C. B. Peirce, University Hospital, Ann Arbor, Mich.
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Roentgen Club
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis.
Meets monthly on last Thursday, October to April, Service Memorial Institute, at 4:30 P.M.

Virginia Roentgen Ray Club
Secretary, Dr. V. W. Archer, University Hospital, University, Va.
Meets annually in October.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1, or as advertised.

Electro-Therapeutic Section of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:30 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Colin Macdonald, Lister House, 61 Collins St., Melbourne, Australia.
Meets monthly at Melbourne during the winter.

Section on Radiology, Canadian Medical Association
Secretary, Dr. A. H. Rolph, 160 St. George St., Toronto, Ont.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale.
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, II.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Virgil Ionescu, B-dul Schitu Măgureanu 49, Bucarest.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6.30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.

THE EASTERN CONFERENCE OF RADIOLOGISTS

The Eastern Conference of Radiologists (composed of the New England Roentgen Ray Society, New York Roentgen Society, Philadelphia Roentgen Society, Roentgenologists of Washington, D. C., and the Radiological Section, Baltimore City Medical Society) held its annual meeting in Baltimore, Maryland, on January 31 and February 1, 1936, with headquarters at the Lord Baltimore Hotel. The program was in charge of the Radiological Section of the Baltimore City Medical Society, with Dr. Charles A. Waters, Chairman and Dr. Whitmer B. Firor, Secretary. Dr. John W. Pierson was Chairman of the Program Committee.

The meeting Friday morning was held in the Hurd Memorial Amphitheatre of Johns Hopkins Hospital, the papers being given by members of the Staff of that Hospital. The first paper was by Dr. Harriet Guild on "Recent Studies in Scurvy." This interesting presentation was illustrated by lantern slides of roentgenograms showing the roentgen findings in scurvy. Dr. Guild pointed out that the most characteristic lesions occur at the ends of the tibia and fibula and the radius and ulna. A number of lantern slides were also shown illustrating the histopathology, and a series showing roentgenograms with accompanying microscopic sections in which it would have been impossible to make a diagnosis roentgenologically without the histopathological study. This work has been published in the *Archives of Disease in Childhood* for August, 1935.

The second paper was given by Dr. Charles F. Geschickter on "The Radioaccessibility of Tumors." Dr. Geschickter pointed out that the primary factor in determining the radiosensitivity of tumors is the tissue of origin. He amplified his talk by a number of charts showing from which embryonal tissue certain tumors originate. From these charts it was possible to determine before beginning irradiation which tumors would respond to treatment. In the last analysis, however, it is not the degree of radiosensitivity of a tumor which determines its radiocurability, but rather the degree of spread at the time irradiation is undertaken. Thus an adequate knowledge of the way and the direction in which malignant disease spreads from a certain location is essential in radiation therapy.

Dr. George O. Gey gave a report on the "Effect of Irradiation on Tissue Cultures." This work was done with Dr. Burnam at the Kelly Hospital. Strains of normal human and animal tumor cells and malignant cells have been maintained for a number of years. When these cells were irradiated it was evident that they were markedly affected. The object of the work was to gain some idea of the maximum period of survival of the cells after they had been exposed to measured doses of roentgen radiation. The technique of irradiation was given in detail. Total doses of from 1,000 to 12,000 r were given, but high exposures, above 12,000 r, would be necessary to destroy viability in some of the cultures. They found that different types of cells from various tumors were affected differently. It is difficult to tell whether the effect of irradiation on tumor cells in the human body is the same as in the experimental work. While the results are inconclusive at the present time, this work is being continued in the hope of obtaining some significant findings.

Dr. J. Earle Moore a very interesting paper entitled "The Value of X-Ray evidence in the Diagnosis of Luetic Aortitis." He pointed out that it is desirable to recognize, if possible, uncomplicated syphilitic aortitis. For many years a great deal of skepticism has existed as to whether or not a diagnosis of uncomplicated luetic aortitis can be made. There are no physical signs or symptoms, or if signs and symptoms are present, they are in effect those which may result from other conditions, such as hypertension. A few years ago Dr. Moore came to the conclusion that in the presence of certain clinical and roentgen criteria it was possible to make a correct diagnosis

in a fairly high percentage of cases. The study reported was based upon a considerable material from the Public Health Institute in Chicago. The conclusion which seemed warranted from this study, from a clinical standpoint, was that dilatation of the aorta as shown in the roentgenogram, does not in itself justify a diagnosis of syphilitic aortitis since it may occur with a fair degree of frequency in the non-syphilitic. The roentgenologist should be in possession of a good deal of clinical evidence, and roentgenoscopy is an essential part of the examination where syphilitic aortitis is suspected. From the clinician's standpoint the roentgen diagnosis of uncomplicated aortitis in the absence of signs or symptoms detectable by the clinician is a hazardous procedure, and to have a reasonable degree of certainty regarding it, the roentgen evidence of dilatation must be backed up by clinical evidence of cardiovascular involvement.

The next paper by Dr. Dean Lewis on "Endothelioma in General" was a very interesting one. He stated that endotheliomas have been variously called angiomas, lymphoepitheliomas, etc. A number of slides representing the different types of endothelial tumors were shown. He included in the group the glomus tumors, which are more frequently found on the hands and particularly under the nails. They are painful and usually of a bluish color and are often wrongly diagnosed as neuromas. The Ewing tumor was also mentioned in his classification of endothelial tumors.

Dr. Stacy Guild gave a talk on "Variations and Developments of the Petrous Bone." A large series of slides were shown demonstrating the histopathology of the petrous bone. Dr. Guild had presented this work as part of a symposium and it has been published in the December number of the *Annals of Otology, Rhinology and Laryngology*. Roentgenologists should be interested in going over this comprehensive work in detail.

Dr. Louis Hamman gave a most interesting discourse on "Acute Fibrosis of the Lung." He presented the reports of four puzzling cases, with slides showing their histopathology and roentgenology. These cases were diagnosed for the most part as bronchopneumonia or tuberculosis. Microscopic study showed that the alveoli were filled with blood cells and albumin, and the interstitial tissue was edematous and swollen. The patients died of suffocation from the fluid in the alveoli. From the clinical factors and anatomical findings a picture appeared of a disease unfamiliar to clinicians and pathologists, and no clear description of the condition could be found in the literature. Apparently there is some infection that occurs followed by inflammation in the lungs, which causes very few symptoms but in an early stage the patient may die from the albumin in the alveoli. A little later this same condition occurs in the interstitial tissue. As the condition advances the patient dies from suffocation in six to eight weeks. As to the cause of the condition, the lungs are sterile and it is impossible to demonstrate any bacteria. This suggests the possibility that the cause may be a filtrable virus.

Immediately after this paper the meeting adjourned and those attending were the guests for luncheon at Sinai Hospital. At two o'clock the meeting re-convened in the Assembly Hall at Sinai Hospital with Dr. Marcus Ostro in the chair. The papers at this session were given by members of the Staff of Sinai Hospital.

The first paper of the afternoon was given by Dr. Charles R. Austrian on the subject of "Encapsulated Hydrothorax resembling Pulmonary Metastasis." This was the report of an atypical case of hydrothorax that filled and emptied and caused confusing shadows in the series of roentgenograms taken. A diagnosis was not made earlier because of failure to take lateral roentgenograms.

Dr. Albert E. Goldstein presented a paper on the "Value of the X-Ray in the Diagnosis of Extrarenal Infections." He stated that since the distribution of organs

around the kidney is so definite it seemed worth while to restudy a number of cases which had been collected in the Genitourinary and Roentgen Departments in the last ten years. From this study they were able to detect certain changes which suggest extrarenal infection. These are as follows: (1) the obliteration of the psoas muscle shadow; (2) the curvature of the spine; (3) the disappearance of the renal shadow; (4) the fixation of the renal shadow when seen; (5) alternation in the outline of the transverse processes; (6) change in the position of the diaphragm. In taking these exposures no special technique was used. The patient is usually placed straight on the table so that no artificial scoliosis is produced. No effort is made to do a pyelogram in the beginning except for differential diagnosis. In this way they were able to study 22 cases of perinephritic abcess. Of the 22 cases, 20 were diagnosed as perinephritic abscess and 18 were verified at the time of operation or autopsy; 2 were not operated upon and 2 were not diagnosed correctly. One finding which appeared in 16 cases at all times was obliteration of the psoas muscle shadow on the side of the abscess. A detailed analysis of the findings in these cases was given. It was also pointed out that stereoscopy is of great aid in diagnosis.

The next presentation was made by Dr. Alexander J. Schaffer on "X-Ray Characteristics of Chronic Lipoid Pneumonia." He stated that a discussion of this condition was important because the diagnosis cannot be made without the roentgenologist and because the roentgenologist has contributed so much to the differential diagnosis. He prefaced his remarks with a short summary of the literature on the subject and gave a report on 41 cases of chronic lipoid pneumonia which have been collected at the Harriet Lane Home in Baltimore since 1930. The disease is apt to appear in very young infants. A summary of the physical signs, pathological and roentgenological characteristics were given, the prognosis being grave. The characteristics of the disease were summarized as follows: (1) the involvement is always bilateral; (2) in this bilaterality the involvement is almost always more pronounced on the right side; (3) it is central in the lobe; (4) it is posterior rather than anterior. There are a number of points which serve to differentiate it from tuberculosis such as no pleurisy; no calcification; no increased peribronchial markings; generally no adenopathy. In conclusion, the author felt that one would be justified in making a diagnosis of lipoid pneumonia in very young children who presented the signs as enumerated.

Dr. William I. Nachlas gave a most interesting paper on "Bone Softening for the Correction of Deformities." He stated that most deformities are believed to develop as follows: (1) the rachitic process produces a bone softening; (2) forces either intrinsic or extrinsic will allow the softened bones to become distorted; (3) the rachitic process is healed either spontaneously or under the care of a physician. Thus the rickets may be cured but the deformities remain. Therefore the deformities must be treated in themselves and not as a part of the rickets alone. In their work they have tried to reverse the process, namely: (1) soften the bones; (2) straighten the deformities; (3) reharden the bones with the limbs kept in a straightened position. The problem was to find a safe method of softening the bones so that their manipulation could be undertaken by hand instead of by surgical methods. The demineralization of disuse was tried but was found to be inadequate. Another process was suggested by some work which had previously been done in the Harriet Lane Home. In some animals which had been fed a high strontium, low calcium, low phosphorus diet the weight of the animal was enough to bow the legs. From this experimental work it was decided to try softening of the bones in rachitic children by a high strontium diet. Eleven cases were so treated. Slides of illustrative cases before and after treatment were shown. A high strontium diet

was administered and after four or five weeks the patient was taken to the operating room and, without anesthetic, the affected bones were straightened and the limbs placed in a cast. Dr. Nachlas described an ingenious device to determine the amount of bone softening. This measured the flexibility of the bones when tension was applied by weights to the center of the shaft, the ends being fixed. The age of the patients ranged from eighteen months to fourteen years. This treatment has been attended by several complications, for instance, in one case a morbilliform rash appeared. However, the results seemed satisfactory, on the whole, and in summary the author stated that there have been chemical studies in addition to roentgen studies to show excretion of the lime salts and replacement by strontium. He felt that in case of fracture of the femur, for instance, which was healed in malfunction, he would prefer to have an osteotomy, with an alignment and cast, but in the case of a patient with many deformities such as occur in fragilitas ossium that has gone on to healing or the deformities of rickets that has gone through to healing or those which do not permit correction by surgery, this bone softening technique permits a correction of the deformities without surgery and with a degree of safety that allows it to be fitted into the armamentarium of almost any good pediatrician.

Dr. Whitmer B. Firor presented an interesting paper on "Roentgen Kymography of the Heart." He gave a short review of the literature and the technique, and showed illustrative cases where roentgen kymography is used. He felt that while in a first examination it may not be of much value, in subsequent examinations it may be of tremendous value in determining whether the heart muscle is developing contractility. He also pointed out the advantages and disadvantages of some of the other methods such as orthodiagraphy, electrocardiography and teleroentgenography.

The concluding paper of the afternoon session was by Dr. Marcus Ostro and Dr. Henry Makover on "Non-parasitic Cyst of the Spleen, with Special Reference to Roentgen Aid in Diagnosis." This was a report of an interesting case which gave some difficulty in diagnosis. Future studies should be made to determine what part the neighboring organs may play in the establishment of a diagnosis in such conditions.

The entertainment provided for Friday evening was an oyster roast held at Lehmann's Hall.

The scientific program was resumed on Saturday morning at the amphitheatre in the new University Hospital, University of Maryland, the papers at this session being given by members of the Staff of the University Hospital. Dr. Henry J. Walton presided.

The opening paper was given by Dr. Harry M. Stein on "Artificial Pneumothorax in the Treatment of Lobar Pneumonia." He said that pneumothorax was not new in the treatment of disease of the lung since it was suggested fifty years before it was ever used. Since it is known that rest of any moving tissue is quite essential for recovery, especially if that part be diseased in an inflammatory way, it would seem reasonable to suppose that any method which would rest the lung would be of benefit. Dr. Stein enumerated the various treatments which have been used in the treatment of pneumonia such as serum, physiotherapy and air conditioning, none of these having lowered the mortality appreciably. He reported 35 cases of pneumonia in which artificial pneumothorax was used. While the cases were not selected, reasonable judgment was used. The results obtained were more satisfactory in children than in the adult group. It was found that not much impression was made on lungs that were consolidated. If too high pressures are obtained fluid develops. The procedure very startlingly relieves pleural pain and the temperature drop is spectacular; within twenty-four to thirty-six hours in some of these patients the temperature dropped to normal. The mortality

in this group was 22.8 per cent. The author concluded that in certain properly selected cases the procedure should be of some value. In discussion it was learned that there was a higher percentage of empyema in the cases treated with pneumothorax.

Dr. Sydney R. Miller gave a very interesting presentation on "Pulmonary Actinomycosis." Statistics from all sources show actinomycotic infections to be rare. A brief review of the literature was given. All evidence points to the fact that when actinomycosis occurs in the human it is due almost exclusively to *Actinomyces bovis*, which is a strictly anaerobic organism, difficult to grow in cultures. While the opinion has been current that the disease is acquired through animal contact or by putting straws in the mouth, the belief is now held by those who have studied the problem that probably this fungus leads a saprophytic existence in the mouth and intestinal tract of human beings since recent work has shown a fairly high percentage of these organisms in the mouth. From this it may be concluded that *Actinomyces bovis* is probably not acquired from sources outside the human body. In a series of cases which have been described throughout the country, three types of lesions are found: (1) those occurring in in the facial region—these make up the majority; (2) those occurring in the abdominal organs, and (3) those occurring in the thorax. This latter means invasion of the chest wall from existing lesions elsewhere. There is no single diagnostic sign which justifies the diagnosis from the roentgen point of view. The roentgen findings can be those that simulate tuberculosis, empyema, bronchiectasis, etc., making a differential diagnosis difficult. During the past year and a half there have come to Dr. Miller's attention three cases in which the disease process seemed to have originated in and been confined to the lung without external manifestations of any sort. The three cases were reported in detail. The finding common in all was that of a rapid onset, with pain localized to the left upper lobe, in a previously well individual, with fever, obscure hemoptysis, high leukocytosis. One case was diagnosed as pulmonary tuberculosis and one as abscess in the left upper lobe. Death occurred in all three and there were no positive findings of actinomycosis until autopsy. The spread of this disease is apparently through the blood stream and not through the lymphatics, since there is no enlargement of the lymph glands as occurs in infection of the ordinary type. Early diagnosis is important from a therapeutic point of view. Therapy can be carried out along two lines: iodides in intensive doses represents the best medical method of approach; in the roentgen literature there is increasing evidence of the efficacy of roentgen therapy, especially in the facial type, to a less degree in the abdominal type and still less in those having the pulmonary type. However, there is a question whether deep roentgen therapy might not be more efficacious if it were instituted earlier, which of course depends on earlier diagnosis.

The next paper was by Dr. Maurice C. Pincoffs on "Diagnosis of Polycystic Disease of the Kidneys and Liver." Polycystic disease of the kidneys and liver is congenital, the mechanism of which is explained by various theories. The occurrence is greater in the female and the condition is observed more often in the first and later years of life. Dr. Pincoffs discussed the subject from the many angles in which the disease presents itself to the clinician. These he divided into the following types, with illustrative cases: (1) the patient who comes to the physician complaining merely of weakness, loss of weight, loss of appetite, vague general symptoms; (2) the patient who comes in simply as a case of hypertension; (3) the case with an unexplained abdominal mass; (4) the case with a recurrent mass on the left side; (5) the group with pain in the side without palpable mass, either right or left; (6) the group with hematuria, usually accompanied by pain so that it suggests a calculous attack rather than renal neoplasm; (7) the group

of cases that have symptoms suggestive of pyonephrosis. In regard to the liver, Dr. Pincoffs stated that polycystic disease of the liver is almost always accompanied by polycystic disease of the kidneys as well and is often diagnosable by determining the presence of polycystic kidneys. With regard to roentgen diagnosis, he felt that intravenous rather than retrograde pyelography should be the method of choice since these patients who are so susceptible to infection should not be subjected to such dangers as are inherent in the retrograde method. Lantern slides were shown of gross specimens of polycystic kidneys.

Dr. Arthur M. Shipley gave a most interesting discussion on "Diaphragmatic Defects." He pointed out the fact that very little space is given in the textbooks to the diaphragm; that with the exception of diaphragmatic hernia little is said about this organ. With regard to the pathology of the diaphragm its defects are the chief concern of the roentgenologist but its position is the chief concern of the surgeon. He pointed out that the diaphragm is not a fixed organ but can assume almost any position in the torso. He enumerated the different pathological conditions which can affect the diaphragm, with illustrative cases. The roentgenologist should always keep this fact of non-fixity in mind. Many conditions such as ascites, pregnancy and tuberculosis raise the diaphragm; it is up and down congenitally and up and down for pathological reasons. Since the pressure within the abdomen is greater than atmosphere and the pressure within the pleura varies from -3 to -7 mm. Hg, the lymphatic current is upward. All inflammations in the abdomen are therefore apt to ascend toward the diaphragm because of this lymphatic current. Dr. Shipley felt that if a little more attention could be given to the diaphragm, the surgeon, clinician and pathologist would be apt to make fewer mistakes.

Dr. J. Mason Hundley, Jr., presented a paper on "The Radiological Treatment of Carcinoma of the Cervix." Beautiful wax models of tumors removed at operation were used to illustrate this talk. The method of treatment is that used by Heyman of Stockholm. The patient is first given a physical examination and then a careful examination of the pelvis. A biopsy is taken from each case. Before starting radiation therapy a blood count is made and a sedimentation test is done. The patient is referred first for roentgen therapy and receives 6,000 to 7,000 r. In three weeks to a month the patient is given radium therapy. Dr. Hundley gave the technique of treatment in detail and reported on 120 cases of carcinoma of the cervix which they had treated; 95 per cent of the cases had squamous cell carcinoma and 5 per cent adenocarcinoma. The majority were between the ages of forty-five and sixty; 11 were under thirty years of age. The cases are classified microscopically using the system of the Memorial Hospital. Lantern slides were shown of microscopic sections illustrating the different types of tumors.

The next paper was by Dr. Grant. E. Ward and Dr. Harry Miller on the "Management of Oral Malignancies." The types of malignant disease which occur in the oral cavity are largely of epithelial origin. The most important part of the therapy is the proper diagnosis and a biopsy is taken from every case if possible. If the lesion is small and can be removed, it is removed by electrosurgery. A Wassermann test is done on every case of ulcerated disease of the mouth. From a careful study of the microscopic sections the method of treatment is determined. The detailed technique and method of treatment of the primary lesion and the glandular metastases were given in detail. Wax models of cases were shown which the authors find of great value in teaching and also in keeping a permanent record of what happens in typical cases. A photographic record accompanies the wax model. Slides were also shown demonstrating the different types of lesions and results of treatment by irradiation.

The last paper on the program was given

by Dr. Howard H. Ashbury on "Treatment of Extrinsic Carcinoma of the Larynx." Slides of charts were presented showing in each patient treated the weight curve, the skin reaction, the time of appearance of the radiation membrane and the total amount of radiation given. This talk was also illustrated by lantern slides showing the patient before irradiation and at the time of the peak of reaction of the skin.

At the close of this session those in attendance were guests for luncheon of the University Hospital.

In the above summary, an attempt has been made to give some idea of what an interesting and valuable program was prepared by the Radiological Section of the Baltimore City Medical Society. The scientific sessions were well attended by about two hundred interested listeners. The arrangements which had been made by the local committees for the guests in the way of transportation, luncheons and entertainment could not have been improved upon. In addition, a spirit of cordiality diffused itself through the two days of the Conference and added greatly to the inspiration furnished by the splendid scientific presentations.

RUTH BIGELOW

ILLINOIS RADIOLOGICAL SOCIETY

A meeting of the Illinois Radiological Society was held at St. John's Hospital in Springfield, Illinois, on January 26, 1936. The session was opened by a two-minute silent tribute to the memory of the late Dr. W. G. Bain, Roentgenologist of the St. John's Hospital in Springfield.

A most interesting program had been prepared by the local committee. Dr. R. K. Campbell presented a paper on the "Indications of Collapse Therapy." This paper was discussed by Dr. Don Deal. A clinical demonstration of lipiodol injection was given by Dr. E. K. Pearson who also presented a number of interesting films depicting the various stages and types of bronchial pathology. At the afternoon session, a paper on "Pyelography" was presented by Dr. Herbert Henkel, and a paper on "Sinus Peribronchial Lymphoadenitis" was given by Dr. H. H. Cole.

Upon the recommendation of the nominating committee, the following officers were elected for the year 1936: Dr. R. K. Campbell, President; Dr. Ivan Brouse, Vice-President; Dr. Cesare Gianturco, Secretary-Treasurer.

CESARE GIANTURCO, *Secretary*

BOOK REVIEWS

Books Received Are Acknowledged under Heading: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

Röntgenology: The Borderlands of the Normal and Early Pathological in the Skiagram. By Alban Köhler, Prof. Dr. med., Wiesbaden, Ex-President and Honorary Member of the German Röntgen Society; Life Member of the British Institute of Radiology and Röntgen Society, etc. Second English edition revised by the author. Translated and edited by Arthur Turnbull, M.A., B.Sc., M.B., Ch.B. (Glasg.), Ex-Demonstrator of Anatomy, University of Glasgow. Cloth. Price, $14.00. Pp. 681, with 400 illustrations. Baltimore: William Wood and Company, 1935.

This is the second English edition of the book which has been frequently described, "as the Bible of Roentgen Rays." This work needs no introduction to American roentgenologists. Not only has the first edition been used as a standard reference and textbook by roentgenologists of this country but it has been published in French, Italian and Spanish. Polish and Hungarian roentgenologists have also sought the opportunity to translate the work into their languages. This edition not only includes the contents of the sixth German edition but also the subsequent advances in medical roentgenology which concern the limits of the normal and the beginning of the pathological in roentgenographic interpretation.

As John Frazer, Regius Professor of Clinical Surgery, Edinburgh, states in his preface to the English edition, the book is a veritable mine of information. The index of contents at the beginning of the volume is arranged in anatomical, topographical fashion. The index at the end contains not only the anatomical areas on which information may be sought but also listing of diseases, symptoms, syndromes, etc. In general, the index is satisfactory but several disadvantages are noticeable. The retention of proper names applied to various diseases, occurs frequently, thus infantile scurvy is listed as such and also as Möller-Barlow's disease. But osteochondritis of the anterior tubercle of the tibia is merely listed as Osgood-Schlatter's disease and not as osteochondritis, epiphysitis, etc. Calvé's osteochondritis of the vertebra, "vertebra plana," is not listed under his name, epiphysitis, osteochondritis, vertebral column, etc. Instances such as these may cause difficulty for a reader or student not conversant with the literature. References to the latter on a given subject are listed in footnotes, and enough are included to enable the searcher to find facts in answer to his questions and to afford a basis for further research. Reproductions of roentgenograms are not great in number, but they have been supplemented in many instances by carefully detailed line-drawings which accurately depict the findings described in the text.

The translation for the most part has been well done, but often the style, as so frequently happens in translation from the German, is stilted, involved and awkward for the English reader. One possible annoyance to the American reader is the frequent use of the term, "roentgen picture" for roentgenogram, etc., and "photographed" for roentgenographed. The editing shows lack of careful revision as manifested by a few references in the text to illustrations in which apparently the wrong number is given.

Slightly more than one-half of the number of pages is devoted to the skeleton, including the skull, mastoids and sinuses. The remainder covers the lungs, thoracic organs, gastrointestinal tract, including the pancreas and gallbladder, and the urinary tract. Cholecystography is included but as stated in his preface, the author has confined his attention to the direct presentation of the organs and systems of the human body and to those contrast methods used daily by the roentgenologist. Thus he has excluded ventriculography, encephalography, pyelography, and others.

It is interesting to note that 18 pages are devoted to a very full and complete discussion of osteochondritis of the metatarsal and eight pages to osteochondritis of the tarsal scaphoid to which Köhler's name has been given, while the other osteochondritides are dealt with in discussions of less than one to four pages. There is no mention of the question of sacroiliac relaxation and no mention of Chamberlain's description of the variation from normal

in the appearance of the symphysis pubis in this condition, although his paper on this subject is quoted in regard to the normal width of the symphysis.

Such defects, as noted, are not of real importance when the monumental and extraordinary scope of this work is considered. Dr. James T. Case says in his preface that there is no other work in any language which contains all the facts pertaining to roentgenologic interpretation so painstakingly and so patiently collected, digested and organized for ready and easy reference. The great and essential feature of the book is the description of the atypical normal, the anomalous and the borderline pathological. Both the young and more inexperienced, and the older more experienced roentgenologist will be spared embarrassing errors in diagnosis and even erroneous testimony in courts of law by constant reference to and study of, this indispensable and voluminous mine of information.

Ralph S. Bromer

The 1935 Year Book of Radiology. Diagnosis, edited by Charles A. Waters, M.D., Associate in Roentgenology, Johns Hopkins University; Assistant Visiting Roentgenologist, Johns Hopkins Hospital. Associate Editor: Whitmer B. Firor, M.D., Assistant in Roentgenology, Johns Hopkins Hospital; Therapeutics, edited by Ira I. Kaplan, B.Sc., M.D., Director, Division of Cancer, Department of Hospitals, City of New York; Director, Radiation Therapy Department, Bellevue Hospital, New York City, etc. Cloth. Price, $4.50. Pp. 580, with 619 illustrations. Chicago: The Year Book Publishers, Inc., 1935.

The 1935 Year Book of Radiology covers the progress of the science during the latter part of 1934 and the first half of 1935. The excellent qualities of the preceding volumes are preserved and the number of abstracts and illustrations is considerably increased. The same editors, leaders in their fields, have carried on the work and the book reflects the value of their wealth of experience and sound judgment.

As Drs. Waters and Firor point out in their introduction to the diagnostic section much of unusual interest was to be found in the literature and there was no paucity of new material. All of the selected articles are important and as the interests of every reader vary greatly any list of so-called "high-lights" is really superfluous. Dr. Waters' own selection of the most interesting features include: the roentgen study of nerves, thorotrast in diagnosis of bone lesions, congenital skeletal conditions, aseptic necroses of the femoral neck, bone-free roentgenography of the eye, contrast media in eye localization, breast roentgenography, expiratory chest roentgenograms, kymography, polisography, congenitally short esophagus, demonstration of pancreatic tumors, signs of intrauterine death, pelvimetry, cephalometry, placenta previa, and endocrine disease.

Dr. Kaplan states that while little of a startling nature has occurred in the field of cancer therapy, so much good and progressive work has been done that the problem of elimination of articles has been a trying one. We find the increasing interest in irradiation of benign tumors and inflammatory conditions well provided for by articles on roentgen therapy in whooping cough, vasomotor disturbances of the lower extremities, ureteral fistula, otorrhea, tuberculous meningitis, angina, salivary fistula, tonsillar hypertrophy and tonsillitis. Articles on radio-diathermo-galvano-therapy and fever therapy alone or combined with roentgen rays are included.

Since only the outstanding contributions to the world's radiological literature for the period covered have been selected, every page contains items of interest and importance. Whoever fails to secure and make use of this volume will have missed the most important and easiest means of keeping his knowledge up-to-date.

E. Walter Hall

The Principles and Practice of X-Ray Therapy. By Ffrangcon Roberts, M.A., M.D. (Cantab.), M.R.C.P. (London), D.M.R.E. (Cantab.), Physician in charge of the Douty X-Ray Clinic, Addenbrooke's Hospital, Cambridge; Examiner in Radiology, Cambridge University. Cloth. Price, 10s.6d. Pp. 214, with 115 illustrations. London: H. K. Lewis & Co., Ltd., 1936.

This well-printed book, which is divided into twenty-four chapters, is an attempt to present the subject of roentgen therapy as concisely as possible. The task of dealing with both the principles and practice of the subject in 214 pages is a difficult one, and its successful accomplishment calls for broad knowledge, ex-

tended experience and exceptional judgment. While in some respects the author has succeeded fairly well, a number of discrepancies tend to diminish the value of his work. For example, it is not clear why a whole chapter should be devoted to hyperthyroidism and only two short paragraphs to bone tumors, only three lines to tumors of the testis, and only four lines to tumors of the kidney. Inflammatory conditions are hardly given the consideration which they deserve. Many subjects are ably discussed and, on the whole, the author's views are sound, but some of the ideas expressed are not in harmony with the experimental data or with the observations of experienced radiologists. In connection with the well-known influence of irradiation on many conditions with which micro-organisms are associated, the author, after explaining that "the existence of a direct lethal action upon micro-organisms so far lacks experimental proof," goes on to say that "we must accept a direct inhibitory action on the organisms as an inescapable fact."

In spite of such occasional lapses, the book is valuable, especially for its description and discussion of various technical methods.

A. U. Desjardins

Classical Contributions to Obstetrics and Gynecology. By Herbert Thoms, M.D., Associate Professor of Obstetrics and Gynecology, Yale University. With a Foreword by Howard A. Kelly, Emeritus Professor of Gynecology, Johns Hopkins University. Cloth. Price, $4.00. Pp. 265, with 58 illustrations. Springfield, Illinois: Charles C Thomas, 1935.

The author of this book deserves the thanks of every obstetrician and gynecologist. He has given us what Long and Fulton have given to other branches of medicine—carefully prepared biographical sketches and intelligently selected gleanings from the masters and pioneers in obstetrics and gynecology.

The author makes no claim for completeness. It was not his intention to completely cover the subject. Instead, by presenting these historical excursions he hopes to stimulate interest in pioneering obstetricians and gynecologists. The author may rest assured that he has accomplished this purpose. His choice of material is largely limited to clinical obstetrics and gynecology and in its selection he has shown a keen sense of judgment. The reader finds common obstetric signs acquiring personality and he is soon lost in comfortable meditation of this elegant little historical panorama.

I have no hesitancy in highly recommending this book. It should find a welcome reception in the library of every obstetrician and gynecologist.

Norman F. Miller

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

NECK AND CHEST

Fellows, Haynes Harold. Significant active pulmonary tuberculosis in the apparently healthy adult; a study of 141 cases. *Am. J. M. Sc.*, Oct., 1934, *188*, 533–537.

An analysis of 141 adults with pulmonary tuberculosis which was discovered during routine fluoroscopy of the chest, shows that 92 per cent were symptom-free or had only one symptom, which was not of itself pathognomonic. By physical examination 42 per cent of the group had râles at either base and 4 per cent had evidence of pleural effusion. Of this same group, 44 per cent had lost 3 or more pounds during the previous year and the weight had remained stationary in 36 per cent. Minimal lesions were shown in 65 per cent of the patients studied, while 30 per cent showed moderately advanced lesions. Of the 131 cases who were treated at a sanatorium 90 had negative laboratory findings, 25 had positive sputum, 12 had a positive guinea pig reaction and 4 had a positive sputum or guinea pig test at some time during their treatment.

From these facts it is evident that early pulmonary tuberculosis may be practically silent and as such it is not only a personal hazard but also a public health hazard.—*G. W. Chamberlin.*

Bönniger, M. Die Lungenspitze im Röntgenstereobild. (Stereoroentgenographic studies of the apex of the lung.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Aug., 1934, *50*, 136–149.

From his study Bönniger concludes that (1) roentgen stereoscopy is of inestimable value in the study of the apex of the lung. (2) By it the dome of the pleura is well demonstrated in normal cases. (3) The dome of the pleura is actually much deeper than is stated by anatomists, not uncommonly it is below the posterior portion of the second rib and the posterior portion of the first rib. The view of the anatomists that the apex of the lung and pleural dome be in the apertura superior is quite incorrect. (4) There is described the typical shadow of the second rib superimposed on the shadow of the dome of the pleura. (5) The shadow described as that of the subclavian artery is that of a thickening of the pleural dome in the apex. (6) The shadow which has been regarded as that of the vena azygos is due to a folding of the pleura.—*E. T. Leddy.*

Wachner, G. Über die Lymphogranulomatose der Lungen. (Lymphogranulomatosis of the lungs.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, June, 1934, *49*, 620–631.

The usual and uncommon types of lymphogranuloma of the lungs are described. They are difficult to classify because they present such a variable picture. There is no roentgenographic typical picture of this lesion, so it is absolutely necessary that a specimen be removed from a lymph node for histologic study so that a definite opinion about the nature of the condition be established. The difficulties of differential diagnosis from carcinoma, lymphosarcoma, tuberculosis, pneumonia, syphilis, etc., are discussed. In this matter the response of the lesion to radiotherapy may offer valuable help. Finally, a complication of lymphogranulomatosis by tuberculosis both from a diagnostic and therapeutic aspect is discussed. —*E. T. Leddy.*

Banting, F. G. Silicosis. *J. Indiana M. Ass.*, Jan., 1935, *28*, 9–12.

The author discusses experimental studies on silicosis and silicotic fibrosis. When fine silica particles are inhaled many of them pass into the terminal air spaces of the lung, where they are phagocyted by the dust cells which lie on the walls of the alveoli. Phagocytes only ingest particles whose diameter is under 6 microns; hence all larger dust particles are harmless. When the monocytes have taken up their load of dust particles, by means of their ameboid movement they pass through the alveolar wall into the lungs. From here they pass into the superficial and deep lymph vessels, the final drainage point being the tracheobronchial lymph glands. Large numbers of dust laden monocytes thus pass into the tracheobronchial lymph glands in individuals exposed to dust,

producing the earliest occurrence of silicotic fibrosis. In the further development this fibrosis interferes with the lymph drainage and the true silicotic nodule appears in the lung tissue. This process is difficult of explanation but it may be assumed that with complete blockage of the lymphatics the monocytes cannot escape with their load of silica; hence they accumulate in groups throughout the lung tissue, lose their ameboid movements, put out processes, and become the fixed connective tissue cells which form the fibrotic nodules, the characteristic lesions of silicosis. The solution of the silicosis problem is one of prevention.—*W. R. Brooksher.*

Dunham, Kennon. Pulmonary emphysema, an important sequela of chronic lung lesions. *South. M. J.*, Jan., 1935, *28*, 32–34.

Pulmonary emphysema is an almost constant sequel of all chronic lung lesions such as tuberculosis, chronic bronchitis, bronchiectasis and silicosis. It is frequently associated with chronic sinusitis. The underlying pathology is damage to the elastic tissue fibers, dilatation of the alveoli, followed by damage to the pulmonary vessels and pulmonary circulation. The diagnostic factors are fully discussed. Roentgenoscopy shows failure of compression of the lung, sharpness of the dome of the diaphragm and limitation of diaphragmatic movement. Stereoscopic roentgenograms are essential for a complete study.—*W. R. Brooksher.*

Goodwin, T. Campbell. Lipoid cell pneumonia. *Am. J. Dis. Child.*, Aug., 1934, *48*, 309–326.

Goodwin reports 2 cases of lipoid cell pneumonia, the roentgen changes of which were reported previously by Pierson (Am. J. Roentgenology & Rad. Therapy, 1932, *27*, 572). In the roentgenograms of these cases the density of the consolidation varied in different parts of the lungs, in this respect being more like tuberculosis than lobar pneumonia. Some areas were so dense as to suggest calcification, while immediately adjacent parts of the lung were so little involved as to cast a shadow scarcely heavier than that of normal lungs. As one proceeded peripherally the density of the consolidation decreased. In lateral roentgenograms there was more involvement of the posterior than of the anterior part of the lung, a point of great importance. Particularly in the extensive cases there was a distinctly "foreign body" type of distribution, with the right side more affected than the left, the upper more than the lower, and the posterior more than the anterior. This coincides with the fact that the greatest incidence of the condition occurs in debilitated infants lying constantly on their backs. Unlike tuberculous infection there was very little enlargement of the mediastinal glands, although a tremendous amount of pulmonary tissue was chronically affected. It is unusual, too, Goodwin says, to see accentuation of the bronchial shadows, particularly at the base, as so frequently occurs in interstitial pneumonia. Pleurisy does not occur if there is no acute pulmonary infection with the lipoid pneumonia, and in most cases not the slightest line of pleural thickening can be seen. Calcification may occur in the tubercle-like nodules scattered throughout the area of consolidation.

A single roentgenogram is scarcely ever typical enough to do more than suggest lipoid cell pneumonia. When, however, roentgenograms taken at intervals show little advance or regression of a lesion with the characteristics mentioned above, lipoid cell pneumonia must be seriously considered. This is particularly true in the absence of tuberculosis or of some other known infection.

Goodwin tabulates the 25 cases reported in the literature, summarizing the histories, etc. He points out the fact that all the children, with one or two exceptions, had some serious illness. On analysis, he found three types of cases.

The first and largest class was made up of cases of meningitis, tumor of the brain, congenital cerebral defects and severe infections with coma or convulsions. In these the loss of consciousness and diminished cough reflex, as well as the supine position, favored the aspiration of foodstuffs or medicines taken into the mouth or regurgitated from the stomach. The second type of case was that of very small infants with debilitating disease causing such weakness as to make vigorous coughing impossible. These babies, if not carefully provided for, lie on their backs, and inert non-irritating substances such as liquid petrolatum easily gravitate to the posterior part of the lung. In the third class vomiting was a most conspicuous feature due to complex causes or simply to improper feeding habits.

The course of the disease in most of the cases

was determined by the conditions associated with it. Goodwin has observed a tendency to improve in his cases. The change was slow, and little difference could be observed from week to week. Scarring of the lung must remain for long periods of time after the oil itself has been phagocytosed and carried away. The rapid respirations gradually diminished and the cough slowly disappeared. Stunting of the growth has so often been associated with the active phase of lipoid cell pneumonia as to suggest it as part of the clinical picture.

Goodwin describes the pathologic process in detail. In the differential diagnosis it must be separated from tuberculosis and other chronic pulmonary infections. It should be suspected in small debilitated infants who fail to gain and have a chronic cough or rapid respiration. The blood picture is usually normal, also the urine and physical examination indicates only that there is some sort of pulmonary consolidation present. The roentgenogram is of the greatest help. In it the consolidation is central, bilateral, more extensive on the right and apt to be posterior. The roentgen density is always more extensive than the amount of consolidation suspected from physical examination. The process is chronic, and roentgenograms taken weeks apart may show scarcely any difference in the appearance of the lungs. The presence of pleurisy and enlargement of the mediastinal glands favor tuberculosis.

The treatment recommended is good nursing with frequent change of position and avoidance of infection of the upper respiratory tract. Goodwin suggests that it is unwise to use drops of oil in the nose of any small or weak infant, and also regards in the same way the use of liquid petrolatum as a cathartic in these babies. When cod-liver oil is poorly taken, he recommends the use of the more concentrated vitamin D preparations. Precautions should be taken in older children to prevent aspiration. Care in feeding and gavage must also be exercised. When children are inclined to vomit they should be placed on their side.—*R. S. Bromer.*

Reinberg, S. A., and Lindenbraten, D. S. Anatomisch-röntgenologische Studien zur Frage von der Pericarditis exsudativa im frühen Kindesalter. (Some roentgenologic and anatomical studies of exudative pericarditis in infants.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, June, 1934, *49*, 598–612.

Among 5,000 post mortems in infants an exudative pericarditis was found in 167 (3.37 per cent) and in only 9 of these was a correct ante-mortem diagnosis made. The authors carried out some investigations of the pericardial sac by injecting opaque medium into some of the corpses of 87 infants up to two years old; into others they injected dilute eosin to open up the pericardial sac and in a third group they sectioned the bodies according to Pirogow's technique. They found that small quantities of fluid always collect at the base of the heart and may so render the shadow of the left border of the heart a straight line; larger quantities collect near the apex. Roentgenologically there were demonstrated small spaces like the pleural sinuses and others were found in the diaphragmatic portion of the pericardium. For the roentgenologic recognition of exudate a change in the configuration of the heart shadow near its mid point is of great importance. Clinically the authors report 45 cases of exudative pericarditis, 40 of which were controlled at autopsy. In 18 cases the roentgen findings were of definite value, in 10 they were doubtful and in 17 the roentgenograms were negative. Roentgen diagnosis is made difficult by the coexistence of other lesions—pneumonia (63 per cent of the cases), pleurisy (65.8 per cent). The text should be consulted for further details of this study.—*E. T. Leddy.*

St. Dedic. Die proportionelle Aortenmessung in der Röntgenologie. (Proportional roentgenologic measurements of the aorta.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, July, 1934, *50*, 42–52.

Proportional measurements of the aorta are of much greater clinical importance than simple measurements of its width. By means of this determination one can evaluate more accurately both normal and pathologic conditions and in cases with widening its degree can be stated. For the proportional measurements of the aorta the following are necessary: (1) A technically exact measurement of the aorta which can be obtained by two direct methods —that of Holzknecht and Kreuzfuchs. The dimensions so obtained are used as the mean in other determinations. (2) The determination of the thorax-aorta ratio. As in normal cases, this is in the proportion of 10 to 1; in other words, the width of the aorta is 1/10 that of the lower thorax. One may therefore decide on the

basis of the width of the thorax whether the aorta in a given case is of normal or pathologic width. (3) The proportional determination of the width of the aorta is of great diagnostic importance. Widths not exceeding the normal by more than 25 per cent are of no clinical importance unless there are other definite reasons for considering disease is present. Widths not more than 30 per cent greater than normal are suspicious. Widths greater than this mean definite disease is present; its severity is in direct proportion to the proportional degree of aortic widening.—*E. T. Leddy.*

Worschitz, F., and von Herman, J. Der Verkalkungsprozess der Aorta im Röntgenspektralbilde. (The process of calcification of the aorta as seen in the roentgen spectrogram.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Sept., 1934, *50*, 307–309.

The roentgenogram of the sclerotic aorta shows additive rings of calcium in which there is decreased interference of the fibers. By the the films it can be shown that precipitation of the sclerosing substance with its crystalline arrangement has an intercellular or intermicellary character. The calcified center in spite of its nuclear content must be regarded as a single substance without any definite arrangement and thereby differ from concretions which form in the human body.—*E. T. Leddy.*

Holst, L. Die Erweiterung des Pulmonalbogens im Röntgenbilde (4 Fälle von Aneurysma der Pulmonalarterie). (Widening of the pulmonary arch as seen roentgenologically; four cases of aneurysm of the pulmonary artery.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Oct., 1934, *50*, 349–360.

The causes of dilatation of the pulmonary arch are quite variable. It is caused by a widening of the root of the pulmonary artery or the conus pulmonalis (rarely by aneurysm of the ductus Botalli). The author discusses the various congenital and acquired conditions that may produce this dilatation, and takes up their clinical and roentgenologic symptomatology and differential diagnosis. Holst discusses this group of cases in which he had 5 of aneurysm of the pulmonary artery, one of which had autopsy control. The differential diagnosis is possible only by careful consideration of all the clinical and roentgenologic findings. Even then it may not be possible to make it. For this reason Holst suggests that all possible cases be reported.—*E. T. Leddy.*

Zierach, H. J. Untersuchungen über die Konstanz der röntgenographisch darstellbaren Bewegungen des Herzens. (Investigations of the constancy of the cardiac movements as seen roentgenologically.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, July, 1934, *50*, 16–29.

Kymographic studies of the movements of any region of the contour of the heart carried out on normal subjects on various days show that the observations remain constant in their extent and nature, if during exposure there is a minimum of inspiration. The presence of air in the stomach does not greatly interfere with the movements but forced respiration gives variable records of the movements. For this reason exposures, to be of value, should be made at the medium position of diaphragmatic movement. The best technical method for controlling this is to make screen examination just before the kymogram is made.—*E. T. Leddy.*

Misske, B., and Schöne, G. Das Herz im Röntgenbilde bei Schilddrüsenüberfunktion. (Roentgenographic studies of the heart in thyroid hyperfunction.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Aug., 1934, *50*, 121–136.

There is considerable difference of opinion in regard to the frequency of cardiac enlargement and of the different sections of the heart in simple goiter and in thyreotoxic goiter. This difference may be explained by the facts that the goiters studied may have varied according to the districts from which the patients came, and that the various authors may interpret similar findings differently. To throw additional light on the controversy, Misske and Schöne report a four-year study they made on 136 patients with goiter, most of whom came from the same region. In this study 160 chest roentgenograms were taken. The cases were divided into ten groups: (1) the mesially situated round heart, 4 cases; (2) the drop-shaped heart, 7 cases; (3) normal-shaped heart, 25 cases; (4) the vertical heart contour, 24 cases; (5) preponderant left-sided hypertrophy and dilatation, 11 cases; (6) spherical form, 9 cases; (7) mitral configurations, 26 cases; (8) bilateral hypertrophy and dilatation, 16 cases; (9) hearts with accentuation of the pulmonary arch with otherwise normal findings, 4 cases,

and (10) auricular fibrillation with "coeur de boeuf," 10 cases. All cases (with the exception of those in the last group) in whom the basal metabolic rate was higher than 50 per cent showed cardiac hypertrophy. This occurred in 44.1 per cent of the cases. There seemed to be no relationship between the duration of the disease and the size of the heart, but there was a relationship between the dilatation and the intensity of the thyreotoxicosis and age. Abnormal curvature of the pulmonary artery found in 36.03 per cent of the cases, especially in the "mitral" and "vertical" hearts, cannot be explained as an isolated dilatation of the right heart, but is an expression of cardiac hypoplasia. Dilatation of the superior vena cava seen in 25 per cent of the cases is not the result of stasis, nor substernal goiter, nor persistent thymus. Further there is no direct relationship between the enlargement of the vein and venous pressure which was increased in the majority of cases. It seems certain that in Basedow's disease constitutional factors play a great rôle in changes in the circulation.—*E. T. Leddy.*

Nolte, F. A. Über die Veränderung der Herzform und -grosse unter der Einwirkung intrapulmonaler Drucksteigerung nach kardiokymographischen Untersuchungen. (Das Kardiokymogramm im Valsalvaschen Versuch.) (The changes in the size and shape of the heart as influenced by increases of intrapulmonary pressure as shown by kymographic examination. (The cardio-kymogram in the Valsalva experiment).) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Sept., 1934, *50*, 211–230.

From his investigation Nolte concludes that: (1) Decrease in the size of the heart regularly follows an increase in intrathoracic pressure of at least 10 mm. Hg. Only in exceptional cases does it occur at a pressure of 35 mm. Hg. (2) This can be observed in either the sagittal kymogram or the first and second oblique diameter. (3) The decrease in size occurs simultaneously in all sections of the heart: an isolated decrease in size of separate sections does not take place during increase of intrathoracic pressure. (4) The decrease in size is most marked around the apex of the heart. (5) The heart decreases in size usually at once during the first heart beat following the increase in intrapulmonary pressure. (6) In about one-third of the cases this decrease in the size of the heart is preceded by a transitory increase during forced respiration which is explainable after the exclusion of other sources of error as due to a displacement by a forced emptying of the blood from the liver and lungs as a result of pressure produced by these organs. (7) With long-continued pressure of about 40–70 mm. Hg there occurs after maintenance of pressure after three to five seconds no further decrease in the size of the heart shadow. (8) Contrary to the views from observation by screen examination and by graphic pulse registration that continued pressure leads to heart stand-still the author observed even with vigorous forced breathing lasting up to twenty seconds constantly a definite pulsation at the margins of the heart. (9) Only with very great differences in pressure (20 and 90 mm. Hg) is there a dependence of the decrease in the size of the heart on the degree of pressure in so far as the heart becomes smaller more rapidly with increased pressure. (10) Immediately the normal intrapulmonary pressure relationships are resumed, the blood streams from the congested veins into the heart, producing increased filling of it and an increase in its size. (11) This increase in size occurs simultaneously in all sections of the heart. (12) Those changes in the size of the heart produced by the Valsalva technique and followed with the kymogram indicate that the decrease in the size of the heart during forced respiration is produced by decreased inflow into it produced by an increase of intrapulmonary pressure and affects both the right and left sides of the heart.—*E. T. Leddy.*

Sabat, B. Zur Geschichte der Röntgenkymographie und Ausarbeitung der Modifikationen der Methode. (The history of roentgen kymography and modifications of the method.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Sept., 1934, *50*, 309–312.

The author, of Warsaw, lays claim to priority of publication on the subject of roentgen kymography because of a paper of his in July, 1911, and he insists that all methods in use at present are modifications of the fundamental principles he discussed.—*E. T. Leddy.*

Weltz, G. A. Die Bewegungen des sagittalen Herz- und Aortenbildes bei der Atmung. (The movements of the sagittal heart and aortic shadows with respiration.) *Fortschr. a.*

d. Geb. d. Röntgenstrahlen, Aug., 1934, *50*, 153–161.

There is considerable uncertainty about the movements of the heart caused by respiration. Holzknecht and Hofbauer stated that the heart is larger in inspiration and that the auricles are enlarged more than the ventricles. Other authors state that there is a decrease in size during inspiration. By means of surface kymography by the method of Stumpf these movements can be demonstrated objectively and by it it can be shown that during respiration two effects working opposite come into play: (1) The respiratory displacement of the heart makes the heart shadow smaller in inspiration. There is an apparent change in the size of the heart which is proportional to the excursion of the diaphragm. (2) The respiratory change in size of the heart is caused by changes in intrathoracic pressure which makes the heart shadow larger in inspiration. The increase in size of the heart is proportional to the variation in pressure. In some cases one and two balance each other so that no change in the sagittal shadow of the heart takes place. Whether the respiratory changes in size are greater in the auricle or ventricle is questionable. The descending aorta, the vena cava superior and the pulmonary arch are shifted laterally if the sagittal heart shadow becomes larger. All movements of respiratory changes in size follow absolutely synchronously. The pulsations of the heart during respiratory changes in size are large with small hearts (in expiration) and with large hearts small (in inspiration).—*E. T. Leddy.*

ABDOMEN

Palugyay, J. Wertigkeit und Auswertung funktioneller Symptome bei Neoplasmen der Speiseröhre und des Magens. (The value and evaluation of functional symptoms in cases of neoplasm of the esophagus and stomach.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, July, 1934, *50*, 3–16.

Before the introduction of studies of the relief of the mucosa of the gastrointestinal tract much weight was placed on functional signs in the diagnosis of organic disease but since then there has been a tendency to use morphologic changes almost exclusively for differential diagnosis. Palugyay, on the other hand, feels that the screen examination by which the function of the various portions of the gastrointestinal tract is best estimated is the most important factor in making diagnosis of organic conditions. The screen examination is therefore of greatest value and importance in the study of the esophagus and stomach. By it a diagnosis of early carcinoma of the esophagus is possible: differentiation of this lesion from other infiltrations of the esophagus can be made. In the examination of the stomach, screen examination allows a differentiation of intra- and extragastric conditions, antral carcinoma from gastritis and finally facilitates the diagnosis of malignant polypi of the stomach.—*E. T. Leddy.*

Schilling, K. Über die Kymographie des Magens. (Kymography of the stomach.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, July, 1934, *50*, 30–36.

Schilling studied a rather large group of patients by means of the technique of Stumpf. By this means it is possible to separate the more passive movement of the upper part of the stomach from the more active peristaltic movements of the lower part. Gastric peristalsis and gastric systole were found to be quite independent and different processes. In pathologic conditions the gastric kymogram shows changes in the movements of the stomach, such as segmental rigidity in ulcer and persisting rigidity in carcinoma. Schilling feels that the gastric kymogram is of definite diagnostic value as it can be utilized without loss of time or money.—*E. T. Leddy.*

Stumpf, P. Zur Kymographie des Magens. (Kymography of the stomach.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, July, 1934, *50*, 37–42.

The graphic study of the movements of the stomach by the surface kymogram furnishes continuous representation of the complicated form and changes of movements at any instant as well as of the slow movements which cannot be seen by ordinary screen examination if the correct grid, a correct speed and correct illumination are used. The gastric kymogram shows: (1) the extent of the movement, that is, the distance between any two end-points; (2) the type of movement of separate points; (3) the difference in time of movement of neighboring points (peristalsis). These characteristics of movement can be easily determined from the kymogram and show well-marked changes in pathologic conditions. In spite of the fact that

gastric kymography has certain limitations, it still is a valuable diagnostic means because of its low cost and simple technique.—*E. T. Leddy.*

Martinotti, Giuseppe. Immagine illusorie di diverticoli del duodeno. (Pictures simulating diverticulum of the duodenum.) *Radiol. med.*, Nov., 1934, *21*, 1266–1286.

Busi described a bend in the lower part of the duodenum to which roentgenologists have given his name; he also called attention to the possibility of opaque paste collecting at this angle and simulating diverticulum of the duodenum. Palmieri said that this is particularly true when the angle lies in a sagittal plane and necessitates a roentgenogram in the lateral or oblique direction to demonstrate it. If, under these circumstances, an anteroposterior roentgenogram is taken the barium may collect in the angle and be visible while the angle itself is not, thus simulating diverticulum. The differential diagnosis of true diverticulum is sometimes possible as there is a small neck connecting the diverticulum with the lumen of the duodenum. But in cases of pseudodiverticulum from traction this differentiation is not possible.

The author describes 6 cases of accumulation of contrast medium in an angle simulating diverticulum. Some of them were at Busi's angle, some at the lower angle of the duodenum and some at the duodenojejunal angle. In half of his cases the apparent diverticula were multiple. He discusses the mechanism of production of these angles and concludes that they are frequently caused by traction from perivisceritis. In such cases the passage through the duodenum is interfered with and there may be a considerable degree of stagnation in the stomach which does not occur in true diverticulitis. These pictures may show the existence of real and persistent dilatations of the kink which may be considered transition forms between mere kink and true diverticulum.

It requires very careful and repeated roentgen examination to differentiate between true diverticulum and the superposition of the shadow of two parts of the duodenum at a bend.—*Audrey G. Morgan.*

Lob, Alfons. Die Ergebnisse nach Übernähung durchgebrochener Magen-Zwölffingerdarmgeschwüre im Röntgenbild. (The results of suture of perforated gastric and duodenal ulcer as seen roentgenologically.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Oct., 1934, *50*, 317.

Repeated roentgen examinations of a number (26) of cases of perforated peptic ulcer treated by simple suture showed that the sutured ulcer could no longer be demonstrated. Suturing may cause immediate changes in the form and position of the inner and outer walls of the stomach. Remote changes are less often seen and are deformities of the stomach at the site of the old ulcer. The diagnosis of gastritis, from changes seen in the walls, must be made with caution because the patient has no symptoms. Healing of ulcer cannot be demonstrated on roentgenologic findings alone, but the diagnosis must be made in conjunction with the clinical findings. The pathologic examination of Lützeler deserves mention in this connection. The author feels that the only indication for a second operation is actual stenosis or the occurrence of a second ulcer.—*E. T. Leddy.*

Pape, Rudolf. Zur Frage der Magenschleimhautatrophie im Röntgenbild bei perniziöser Anämie. (Atrophy of the mucous membrane of the stomach as seen roentgenologically in pernicious anemia.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Oct., 1934, *50*, 327–336.

The author studied roentgenologically the atrophy of the gastric mucous membrane—a hitherto much neglected subject—in 45 patients with pernicious anemia. The elasticity of the folds of the mucosa is more important than their caliber for this may vary with different factors such as the degree of filling of the stomach, the gastric tone, compression, position of the stomach in relation to the position of the patient, etc. The abnormal ease with which the folds may be obliterated, even with moderate filling and slight compression, indicates a delicate thin mucous membrane even when the folds do not appear unduly delicate. A widening of the folds with the patient in the horizontal position over their size with the patient erect does not count against atrophy for the question of atrophy cannot be settled by roentgen examination alone. Folds that could be obliterated with abnormal ease were demonstrated in half the cases of pernicious anemia and in one-fifth of control cases. "Atrophic relief loss" (atrophisches Reliefschwund) described by Chaoul was not demonstrated in these cases and Pape thinks it occurs only in

atrophic-hyperplastic gastritis. Hyperplastic changes are seldom seen in pernicious anemia, but they were observed in 2 cases of gastric cancer with associated pernicious anemia. If hyperplastic gastritis precedes carcinoma (primary gastritis) the observance of the hyperplastic mucosal changes of pernicious anemia is very important. By such a control in a few cases an early diagnosis of cancer with pernicious anemia can be made more often than has previously been possible.—*E. T. Leddy.*

Gutzeit and Kuhlmann. Über die Symptomatik der Ulcera ventriculi an der grossen Kurvatur. (The symptomatology of ulcer on the greater curvature of the stomach.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, June, 1934, *49*, 613–620.

According to the authors' observations, gastric ulcer of the greater curvature has a characteristic roentgenologic symptom-complex. On the one hand, there is the cover or pack-fold symptoms (Deck- oder Packfaltensymptom) and their distinction from filling defects due to tumor, and on the other hand, the transverse folds of the rugae as symptoms of ulceration near the greater curvature, and the authors state that from the roentgen findings alone it is possible to make a differential diagnosis of benign ulcer of the greater curvature from other lesions such as carcinoma or adhesions which may produce a similar niche. They also discuss conditions leading to para-ulcerative changes in the greater and lesser curvature.—*E. T. Leddy.*

Leithauser, Daniel J., and Cantor, Meyer O. Solitary intramural fibroma of the pylorus. *J. Mich. M. Soc.*, Jan., 1935, *34*, 15–17.

The authors report in detail a case of solitary intramural fibroma of the pylorus, discussing the pathology and symptomatology. The roentgen examination disclosed a persistent lengthening and narrowing of the pylorus without filling defect. Recognition of benign gastric tumors is most important. They should be suspected in any case in which the gastrointestinal symptoms are not characteristic, especially in the presence of indefinite roentgen findings.—*W. R. Brooksher.*

Kessler, Emma. Das Magensarkom. (Sarcoma of the stomach.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Sept., 1934, *50*, 247–263.

One of the characteristics that may distinguish a gastric sarcoma from a cancer is the fact that it (the sarcoma) usually occurs at an earlier age. Its localization also is different in that in one-third of the cases it occurs on the greater curvature. In one-fourth at the pylorus, and in one-fifth on the lesser curvature. Kessler points out that a diagnosis of gastric sarcoma cannot be made. She reviews the histories and histologic findings of reported cases. Extragastric tumors with extensive deformity of the wall of the stomach are easily recognizable as sarcomas. Lymphosarcoma and round cell sarcoma offer the greatest difficulty. A tentative diagnosis can be made in many cases with the assistance of the clinical findings. This paper has an extensive bibliography.—*E. T. Leddy.*

Grilli, Adamo. Contributo allo studio clinico-radiologico dell' ulcera peptica post-operatoria. (Clinical and roentgen study of postoperative peptic ulcers.) *Radiol. med.*, Dec., 1934, *21*, 1361–1384.

Seventeen cases of postoperative peptic ulcer, 11 of them verified by operation, are described and illustrated by roentgenograms. The diagnosis was made by roentgen demonstration of a niche which is the only definitely reliable sign. None of the indirect signs are reliable. A number of cases are described in which mistaken diagnoses were made on the basis of indirect signs; the incorrectness of the diagnosis was shown by operation. The atonic appearance of the loop containing the anastomotic opening with disappearance of the mucous folds is not constant but changes with return of tonus of the loop. Schinz has recently described as a new indirect sign a total or segmental spasm of the transverse colon caused by inflammation of the mesocolon near the ulcer; but this is not any more constant than the other indirect signs.

The niche in postoperative peptic ulcer does not differ morphologically from that in gastric or duodenal ulcer. The appearance differs depending on whether it is looked at in profile or from in front; in the latter case the mucous folds converge toward it like arrows indicating the lesion. A small amount of paste should be used, distributed by graduated compression, so as to show the mucous membrane relief. A short exposure time should be used. The opaque shadow of a true niche persists on compression while that of a false niche disappears; however, false niches may persist for some

time and true ones may be transitory, so a very careful examination is necessary with repeated roentgenograms. A niche which does not appear on a first examination may appear on another roentgenogram taken several days later.—*Audrey G. Morgan.*

Gabor, Marcell E., and Hiller, Robert I. Primary carcinoma of the jejunum. *Am. J. Surg.*, Jan., 1935, *27*, 121–125.

Carcinomas of the small intestine are usually adenomatous in type, annular in distribution, and produce varying degrees of obstruction. Metastases and involvement of adjacent organs by direct extension occur relatively late. No positive diagnostic points are elicited and the symptoms are directly related to the degree of obstruction which is present. Roentgenological study determines the presence and location of the tumor. Repeated examinations to observe the passage of the opaque meal are necessary to visualize the lesion. The differential diagnosis is fully discussed. The indicated treatment is by surgery. A case is reported in detail. —*W. R. Brooksher.*

Dall'Acqua, Virgilio, and Valsecchi, Romeo. L'aspetto radiologico della mucosa del colon negli stati patologici. (The roentgen appearance of the mucosa of the colon in pathological conditions.) *Radiol. med.*, Nov., 1934, *21*, 1213–1252.

The modern method of examination of the colon by means of an enema with small amounts of contrast fluid has as its object to study the mucous membrane relief of the intestine. It shows the importance of the folds of the mucous membrane as a factor in digestion. The relief is very unstable, changing with the varying phases of digestion and showing the autonomous movement of the mucous membrane.

The changes which take place in the mucous membrane relief in acute and chronic inflammation, diverticulosis and diverticulitis, intestinal polyposis, malignant tumors and stenosis in general are described in detail and profusely illustrated with roentgenograms. Such examinations show the extent, nature and to a certain extent the gravity of the lesions. In mild forms of colitis there may be no change in the mucous membrane relief. The enema also gives information in regard to the motor function of the colon which is shown by the response of the walls of the colon to the stimulus of the enema. In atony the colon distends readily without causing any impulse to evacuation; there are few haustra. Evacuation is brought about almost completely by contracture of the abdominal muscles and vis a tergo. In hypertonia the colon is contracted, there are many deep haustra and sometimes spasms. The progress of the enema may at first be slow and difficult and it may then rise suddenly to the proximal colon or even to the cecum. Anomalies in the evacuation of an enema may be due to incoordination between the nerves of the right and left halves of the colon.

If evacuation of the enema is incomplete and it is impossible to obtain a good roentgenogram the method of small centered roentgenograms with graduated compression may prove successful. Examination with complete distention should also be made to supplement the study of mucous membrane relief.—*Audrey G. Morgan.*

Piccinino, Guido. Salto di Stierlin e tubercolosi intestinale iperplastica. (Lack of contrast filling of the cecum and ascending colon in hyperplastic tuberculosis of the intestines.) *Radiol. med.*, Nov., 1934, *21*, 1253–1266.

Five cases of hyperplastic tuberculosis of the intestine are described and illustrated with roentgenograms. All of these have certain roentgen signs in common. In all the pathological lesions began in the last loop of the small intestine which was extremely deformed with varying degrees of stenosis and manifest signs of rigidity. The cecum and ascending colon were greatly constricted in all the cases, though to different degrees in the different ones. They looked as if they had been enveloped and compressed gradually by some force acting on them from outside. There was more or less complete lack of filling; there was enough filling to show the mucous membrane outline which had lost its normal folds and instead showed an irregular design, in some cases flaky. Here and there, there were some small extroflexions that looked like ulcer niches or intramural diverticula. While the contents passed through quite rapidly there was no evidence of muscle contractions but the appearance of rigidity.

The two conditions from which this hyperplastic tuberculosis must be differentiated are malignant tumor and chronic appendicitis.

There were none of the clinical signs of tumor in any of these cases. In cancer the lumen of the intestine appears to be deformed rather than constricted, the lesion is more circumscribed and the boundary between the normal and pathological parts is sharper. The mucous membrane design is completely lost or there are only a few irregular rigid folds. There is never the areolar or flaky appearance that there is in tuberculosis.

The clinical signs of chronic appendicitis are more like those of hyperplastic tuberculosis and might even be confused with them. But the roentgen changes are strictly limited to the cecum, generally to its base and do not extend to the ascending colon; in the terminal loop of the ileum there are functional changes but not true anatomical changes. The mucous membrane folds are preserved but are turgid and thickened. A comparison of roentgenograms from cases of chronic appendicitis and hyperplastic tuberculosis clearly shows the differences.—*Audrey G. Morgan.*

Davis, A.A. Hypertrophic intestinal tuberculosis. *Surg., Gynec. & Obst.*, May, 1933, *56*, 907–913.

Tuberculosis of the intestine according to the "French" classification consists of (1) the ulcerating type or tuberculous enteritis; (2) the stenosing type; (3) the enteroperitoneal type; (4) the hypertrophic type. Types 1 and 2, being invariably secondary to phthisis in adults and forming the bulk of the intestinal cases in children, constitute the overwhelming majority of all cases of intestinal tuberculosis.

The author describes 29 cases of the hypertrophic types of tuberculosis of which all but 3 were proximal to the hepatic flexure, these 3 involving the sigmoid. In 1 case the jejunum was involved, a very unusual site of involvement by tuberculosis of the hypertrophic type. The average age was thirty years, which corresponds closely to other series. It is a generally accepted view that hypertrophic tuberculosis is usually primary in the intestinal tract, particularly in children. Weber and Tante found the bovine variety of tubercle bacilli in 25 of 28 cases of primary intestinal tuberculosis.

Various symptoms are exhibited which result from a subacute intestinal obstruction with intermittent attacks of intestinal colic. There is a tendency to constipation with very occasional attacks of diarrhea. The duration of symptoms is usually over a long period of time. There is a palpable tumor in 65 per cent of the cases. Blood and slime are discharged from the rectum.

Treatment of hypertrophic intestinal tuberculosis, in contrast to the other three types, is surgical. Although some authors recommend resection, Davis reports very gratifying results by merely an ileocolostomy.—*J. H. Vastine.*

Bejul, A., and Holst, Leopold. Die Röntgendiagnose der chronischen Appendizitis. (The roentgen diagnosis of chronic appendicitis.) *Fortschr a. d. Geb. d. Röntgenstrahlen*, Oct., 1934, *50*, 344–349.

Every normal appendix can be filled with contrast medium. If it does not fill when a suitable technique is used this finding is pathognomonic of chronic appendicitis. An incompletely filled appendix is of some importance for the diagnosis of chronic appendicitis. A tender point in the region of the appendix, especially when it cannot be filled or is incompletely filled, is pathognomonic. A limitation of movement of the appendix, especially when other symptoms are present, means appendicitis. Changes in the cecum and ileum are secondary indirect signs. A regular filling of the appendix without a tender point means a normal appendix. Changes in its shape without fixation and pain have no meaning. The authors feel that roentgen examination should be made in all suspected cases of appendicitis as it facilitates the diagnosis and gives valuable indications about the operative procedures to employ.—*E. T. Leddy.*

Ottonello, Pietro. Visibilita radiologica della papilla di Vater in soggetto con nicchia duodenale. (Roentgen visibility of Vater's papilla in a subject with duodenal niche.) *Radiol. med.*, Jan., 1935, *22*, 25–27.

A case is described in which Vater's papilla was visible in the roentgenogram of a patient who had a duodenal niche. From this and 2 similar cases that he has observed and from experiments on dogs, the author concludes that at least some cases of ulcer of the duodenum may be caused by spasm of the sphincters of the common and pancreatic ducts, this spasm being demonstrated by visibility of Vater's papilla in the roentgenogram. It will require further study to clear up more accurately the relation between peptic ulcer and visibility of Vater's papilla.—*Audrey G. Morgan.*

Oughterson, A. W., and Mendillo, J. C. The effect of peritoneal irritation on the emptying time of the gall bladder and stomach. *Surg., Gynec. & Obst.*, June, 1933, *56*, 1013–1016.

The authors determined the emptying time of the stomach and gallbladder following the intravenous administration of sodium tetraiodophthalein, and the emptying time of the stomach following administration of barium. The peritoneum was traumatized by rubbing the ileum briskly with gauze or by cauterizing the appendix, and subsequent examination showed a definite delay in the emptying time of the stomach and gallbladder. Hughson found a similar delay in emptying of the stomach following peritoneal irritation and Birch and Boyden demonstrated a delay of the emptying time of the gallbladder following faradic stimulation of other portions of the gastrointestinal tract. It is suggested that certain types of gastric and gallbladder dysfunction and stasis may be explained on the basis of these reflex pathways from disease elsewhere in the gastrointestinal tract.—*J. H. Vastine.*

Berner, F., and Meythaler, F. Röntgenologischer Nachweis der Perforationswege von Leber- und Milzechinokokken. (The roentgenologic demonstration of the path of perforation of ecchinococcus disease of the liver and spleen.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Oct., 1934, *50*, 337–343.

This is the report of a case of spontaneous perforation of an echinococcus cyst of the liver into the biliary tract with the passage of several cysts by bowel. With a fair degree of certainty the probable route of perforation could be demonstrated roentgenologically. Another case of spontaneous perforation of a cyst of the spleen into the left flexure of the colon is described in which the route of perforation was definitely shown roentgenologically. In a third case, operated on repeatedly for ecchinococcus disease of the liver, the diagnostic value of the kymogram was demonstrated.—*E. T. Leddy.*

Hartung, Adolph, and Wachowski, T. J. A modified technique for suspected gall bladder disease. *Illinois M. J.*, Jan., 1935, *67*, 71–76.

Oral cholecystography followed by an opaque meal for the demonstration of possible secondary signs is advocated as particularly valuable where questionable cholecystographic findings are obtained. The method further permits the demonstration of pathology other than of the gallbladder which may be present simultaneously, or which may be responsible for symptoms simulating those of gallbladder disease.—*W. R. Brooksher.*

Hershenson, Morris A. The differentiation of confusing shadows in cholecystography. *Am. J. Digest. Dis. & Nutrition*, Jan., 1935, *1*, 799–801.

To produce cholecystograms of maximum diagnostic value, the gallbladder image must be placed away from interfering superimposed shadows. The author accomplishes this by shifting the roentgen tube as for stereoscopic films employing a shift about twice as great. The resulting films are viewed separately. Illustrative roentgenograms and diagrams are presented.—*W. R. Brooksher.*

Raiford, Theodore S. Epitheliomata of the lower rectum and anus. *Surg., Gynec. & Obst.*, July, 1933, *57*, 21–35.

Anorectal epitheliomata constitute 3 to 4 per cent of all rectal malignancies. The author reports on 10 cases; the average age at which they were first observed was 48.7 years, and 8 of the 10 patients were females. The most common premonitory symptoms were itching, pain, bleeding and a palpable mass. Diagnosis is made microscopically but differentiation must be made clinically from nonspecific ulcer, tuberculosis, eczema, fissures and fistulas, venereal warts and condylomata, melanomata, lymphangiomata, endometriomata of the rectovaginal septum, old hemorrhoids and anomalies of the proctodeum and coccygeal vestiges.

Regarding their location they may be classed as internal or external according to their origin from within or without the anal sphincter. Morphologically they may be classed as nodular or ulcerating. The nodular, indurating growth represented, in the majority of cases, a histological type characterized by cells growing throughout the subcutaneous and submucous tissues in a discrete, well-circumscribed manner but showing active mitoses. This is the more malignant type. The second was commonly composed of diffusely invading cells of a pure squamous type with few mitoses and many epithelial pearls. Metastases from anal epitheliomata usually appear first in the inguinal

nodes, later involving the glands of the perirectal tissues, the mesorectum and the sacral glands.

Treatment. Surgical extirpation, while removing the primary tumor, is frequently followed by reappearance of the growth or metastases to the inguinal nodes. Monod, of the Institut du Radium, in Paris, considers these tumors more radiosensitive than carcinomata of the rectum. Gordon-Watson, of London, compares the sensitivity of these tumors to that of epitheliomata of the tongue and reports optimism over the results of irradiation in a few personal cases. Binkley, of the Memorial Hospital, New York, advocates heavy external irradiation in preference to the interstitial method because of the severe reaction which not infrequently follows the latter. He feels that this, followed by excision, constitutes the most favorable mode of treatment. Lenz, at the Presbyterian Hospital, New York, advocates massive doses of radiation preoperatively. Raiford, recommends external irradiation followed by radical excision.—*J. H. Vastine.*

Boyden, Edward A., and Fuller, Alice H. Anatomy and physiology of the gallbladder in children; a cholecystographic study. *Am. J. Dis. Child.*, Sept., 1934, *48*, 565–579.

This study consists primarily of a comparison of the evacuation of the gallbladder in children with the emptying of that viscus in young adults, and is the continuation of a preliminary study made several years ago. The method employed was to visualize the gallbladder by the administration of tetraiodophenolphthalein, from 2 to 3 gm. in grape juice given in two successive doses the night before roentgenograms were to be made. The next morning after preliminary films were exposed, the patient was given a glass of milk in which three egg yolks were stirred. Roentgenograms were then made, 2, 4, 8, 12, 16, 20, 25, 30, 35, 40, 50, and 60 minutes after the ingestion of the food. No exposures were made after one hour.

Forty-one children between the ages of six and eleven years were subjected to this technique. Owing to difficulties of making roentgenograms of children of this age, only 28 of the series of 41 were available for statistical study. After the outlines of 400 of the gallbladder shadows were transferred to tracing paper, the volume of the fundus, body and infundibulum was computed by means of a graphic method which Boyden described in a previous publication.

Under the most favorable circumstances, the iodized bile outlined the cystic duct as early as eight minutes after the ingestion of food; in one patient, six minutes after the ingestion; and in another it was visible before food. This is consistent with previous findings, namely, that in young adults the soonest that bile from the gallbladder may be aspirated from the duodenum is seven minutes after a glass of egg yolk has been swallowed.

In these children it was possible to make lateral roentgenograms of the gallbladder. From both angles, anteroposterior and lateral, study of 8 cases indicated that in the prone position the gallbladder usually slopes forward (from above downward), forming an acute angle of less than 30° with the adjacent portion of the spine. The lateral views also showed that the infundibulum bends to the left (in passing upward) within the plane of the posteroinferior surface of the liver, but that it does not bend anteriorly or posteriorly. The neck of the bladder, however, bends both to the right and forward as it extends upward.

The authors draw two conclusions from these observations: (1) that the computation of volumes made from the prone views are frequently based on foreshortened images and therefore provide an underestimate of absolute volume, and (2) that since the shape of the gallbladder in cross-section varies with the individual—being round in some patients and in others compressed either from side to side or anteroposteriorly—the absolute volume cannot be successfully computed in the absence of data concerning both diameters, but the rate of emptying is the same whichever view, lateral or prone, is being used for computation. This would tend to disprove the theory of emptying of the gallbladder by means of malforming agencies such as the pressure of food in the stomach or duodenum, or the peristaltic action of either organ, as has been recently advocated.

In plotting the rate of emptying of the viscus in children, the authors found that in general the curves of emptying are much like those in adults, except that the initial volume was not so large. The principal period of discharge occurred within the first forty minutes after ingestion of food. The "two minute pause" (a characteristic delay in emptying, between two

and four minutes after the meal) also occurred in children. Also, a reversal of the usual reaction to food was sometimes encountered, as instances of gallbladders that relaxed before contracting, thereby appearing temporarily larger in volume than before the egg yolk was ingested. Approximately 27 per cent of the contents of the gallbladder was discharged in the first eight minutes, 45 per cent after twelve minutes, 64 per cent after twenty minutes, 75 per cent after thirty minutes and nearly 80 per cent by the end of the first forty minutes. The two lowest readings occurred in children admitted to the hospital for treatment of icterus and obscure abdominal pain; a case of gastrointestinal disturbance gave the lowest reading at forty minutes in boys and a case of migraine gave the third lowest reading at the same time in girls. Conditions such as osteomyelitis, epilepsy, muscular weakness and traumatic conditions, apparently did not influence the emptying.

In regard to sex it was found that a reversal of sex differences occurs in children as compared with young adults, owing to progressive slowing of the rate of discharge of the gallbladder of boys as they pass from the period of childhood to youth. There was no significant change or difference in the emptying time of girls and women. The cause of the slowing of evacuation in boys is not obvious. It is believed that these differences are to be interpreted primarily on the basis of changes taking place in the upper portion of the intestinal tract.—*R. S. Bromer.*

GYNECOLOGY AND OBSTETRICS

Buchner, Edward F. Undistorted radiography in obstetrics. *J. Tennessee M. Ass.*, Jan., 1935, *28*, 30–31.

Lateral teleroentgenograms are advocated for diagnostic obstetrical roentgenography as a means of avoiding distortion. The most important measurements may be taken direct from this film.—*W. R. Brooksher.*

Ude, Walter H., and Urner, John A. Roentgenologic diagnosis of placenta previa. *Minnesota Med.*, Jan., 1935, *18*, 9–11.

Report is made of the roentgenological study of 35 patients presenting abnormal uterine bleeding in the third trimester of pregnancy, of whom 14 showed roentgen evidence of placenta previa. In all cases there was corroboration of roentgenological findings by clinical and, in some cases, by operative findings. In the technique employed not over 40 c.c. of sodium iodide or other contrast solution is injected into the catheterized bladder, thus clearly defining its upper margin. The placental mass is identified by its relationship to the urinary bladder and other pelvic structures. Normally, the uterine body rests against the upper posterior side of the urinary bladder. With the technique employed, the normal soft-tissue space between the fetal cranial bones and the contrast medium scarcely exceeds 1 cm. in diameter, being demonstrated as a narrow band of tissue between the two landmarks. In placenta previa, however, the space is considerably wider and the placental mass will usually be defined in outline on the film. The fetal head must, of course, present in the lower uterine segment for the application of the method. An opinion may be expressed as to the presence of a central or a partial type of placenta previa by a consideration of the size and position of the placental mass and the nature of the displacement of the fetal head. Blood clots or the interposition of a foot or a hand may confuse the interpretation. For accurate diagnosis, the roentgen findings must therefore be corroborated by the clinical and physical data.—*W. R. Brooksher.*

Bland, P. Brooke, Goldstein, Leopold, and Bolton, William W. Compound intrauterine and extra-uterine (lithopedion) pregnancy. *Surg., Gynec. & Obst.*, May, 1933, *56*, 939–942.

The subject of lithopedion is discussed and a case presented in which there was a combined intrauterine and extrauterine pregnancy. Patients are often entirely unaware of any abnormal abdominal condition, the extrauterine pregnancy (lithopedion) being discovered roentgenologically as an incidental finding.

Küchenmeister classifies calcified fetuses as (1) lithokelyphos, those in which the membranes and lymph undergo fatty degeneration and calcification with a resulting stone-like capsule about a degenerated fetus; (2) lithokelyphopedion, in which the fetus and sac both show widespread infiltration with lime salts, and (3) lithopedion (stone child or lithotecnon), which includes in general all types of calcified fetuses and particularly those in which the fetus itself undergoes organization

and massive calcification. A true lithopedion forms when the fetus escapes unattached into the peritoneal cavity with or without the enveloping membranes. A compound pregnancy means the combination of an intrauterine gestation associated with a long standing mummified or calcified fetus in the abdominal cavity. Not infrequently an intrauterine gestation commences synchronously with an extrauterine one.—*J. H. Vastine.*

GENITOURINARY SYSTEM

Rose, D. K., Hamm, William G., Moore, Sherwood, and Wilson, Hugh M. Kidney pelves; normal variations in their shape and flow with possible pathological significance. *Surg., Gynec. & Obst.*, July, 1933, *57*, 1–14.

It has long been recognized that anomalies of the kidneys or ureters predispose to disease. The authors have grouped borderline types of pelves which, while classified as normal might, in the process of emptying, permit either constant or temporary stasis of small amounts of urine, in all or in certain portions of the kidney pelvis, and which apparently predispose the organ to any of the pathological chances in which stasis is a recognized etiological factor. These pelves they have termed "dysuric." Forty-one cases of renal calculus were studied, in 33 of which a dysuric type of pelves was found. Of 33 nephralgic kidneys without other demonstrable cause for the pain, 31 showed varying degrees of dysuric pelves. In 43 cases with symptomatic nephroptosis, 29 showed dysuric types of pelves. In 11 cases of renal tuberculosis a dysuric type of pelves was found in 9. Of 10 examples of idiopathic or essential hematuria, 7 had a dysuric type of pelves. This classification of dysuric and non-dysuric types of kidney pelves is one in which a rather large personal equation can possibly enter.—*J. H. Vastine.*

Henline, R. B. Renal tuberculosis. *Surg., Gynec. & Obst.*, August, 1933, *57*, 231–241.

It is estimated that 0.5 per cent of all operations and 27 to 30 per cent of kidney operations are performed for renal tuberculosis. This is a disease of early adult life, more than half the cases occurring between the ages of twenty and forty. In the author's series of 34 patients, bladder symptoms were present in 85.3 per cent, pain in the kidney region was a prominent symptom in 76.5 per cent, cloudy urine in 50 per cent, hematuria in 44 per cent and general symptoms in 35 per cent; tubercle bacilli were found in the urine in 47 per cent of the cases. A few pus cells in the urine of an individual between twenty and forty years (excluding venereal disease) should make one suspicious of renal tuberculosis.

Diagnosis is based primarily upon the irregularity or filling defect in the pyelogram. In the author's series of cases pyelograms were considered diagnostic in 82.3 per cent. There are two common types of advanced renal tuberculosis which may ordinarily be diagnosed by the pyelogram. The first appears as a large, dilated, irregular kidney pelvis, and a megaloureter. This type usually has very poor renal function and is the end-result of a continuously destructive process. The second type is characterized by shagginess and irregularity of the major and minor calyces, without much increase in the size of the kidney pelvis, often with calcifications in the kidney substance, and a small irregular beaded ureter. This latter group includes those cases which show a tendency toward healing, and usually have a better resistance to tuberculous infection.

The author recommends retrograde bilateral pyelograms routinely if the ureters can be catheterized. Intravenous urograms are particularly valuable in those cases in which it is impossible to catheterize one or both ureters. The function can be determined by this procedure but it often fails entirely to outline the minor deformities in early cases and is therefore of less value as a routine measure than retrograde pyelograms.—*J. H. Vastine.*

Töppner, Rudolf. Die diagnostische Bedeutung des pyelovenösen Refluxes. (The diagnostic importance of the pyelovenous reflux.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Sept., 1934, *50*, 281–286.

Two cases are cited where the veins were demonstrated by retrograde pyelography. The observation of the pyelovenous reflux has no pathognomonic importance. It merely indicates an increased pressure in the kidney pelvis.—*E. T. Leddy.*

Worschitz, F., and von Herman, J. Feinstruktur-Angaben zur Harenstein-(Urat-) Bildung. (The study of the fine structure of urinary calculi (urate stones).) *Fortschr. a. d.*

Geb. d. Röntgenstrahlen, Sept., 1934, *50*, 305–307.

The crystal structure of urate salts was investigated by roentgenograms. These were made of polished surfaces of the globular stones in a tangential and radial direction. The roentgenograms showed that the crystal structure is a polycrystalline aggregate with the crystals arranged radially. The aggregation center of urinary calculi can be regarded as a geometric center of the axes of the coarse crystals which are deposited radially, and the highest tension occurring in this direction.—*E. T. Leddy.*

Kutzmann, Adolph A. Diverticulum of the urinary bladder; an analysis of one hundred cases. *Surg., Gynec. & Obst.*, May, 1933, *56*, 898–906.

Diverticulum of the urinary bladder is the result of both congenital and acquired anatomical factors. They occur most frequently in men—97 per cent—and they occur in 1.2 per cent of general urologic cases. Most cases were found in later life, 91 per cent of the author's 100 cases being in patients over fifty years of age. Microscopically the walls of the diverticula are composed of fibrous tissue with chronic inflammation. A living epithelial membrane was present, with only occasional muscle fibers being seen.

The causes are classified as true diverticula and false or incipient diverticulosis. The true diverticula are more commonly single and larger in size, exhibiting a definite orifice, having an anatomical sac-like structure, and situated in the region of the ureters. The false or incipient diverticula are for the most part cellular or shallow wide-mouthed depressions due to the protrusion outward of the epithelial lining between hypertrophied muscle bundles and are nearly always multiple and found throughout the bladder.

There is no distinctive symptomatic syndrome. The most frequent symptoms were frequency, difficulty, nocturia, dysuria, dribbling and burning with complete retention in about one-fourth of the cases. The outstanding symptomatology is the long duration. Diverticula are usually secondary to urinary retention. The retention was due to prostatism in 64 per cent of the author's cases, median bar in 18 per cent, carcinoma in 5 per cent, urethral stricture in 3 per cent, and carcinoma of the bladder in 2 per cent. Urinary calculi were present in 16 of the 100 cases.

Diagnosis of diverticula is by cystoscopy and roentgenograms. Opaque cystograms are made, following which it is often helpful to withdraw the opaque medium and introduce air into the bladder—pneumocystography. The true diverticula are seen as single or multiple, smoothly outlined, shadows projecting beyond the lumen of the vesicle wall. The false or incipient diverticulosis is seen on the cystogram as a rather extensive irregularity of the bladder which upon close inspection is seen to consist of innumerable small projections of varying sizes.

Treatment consists in correction of the obstructing factors, only such diverticula being individually treated as may be of the retention type, or of a large size. Correction of the obstruction relieves the patient's symptoms but there is no change in the size of the diverticulum proper.—*J. H. Vastine.*